Available online at www.sciencedirect.com
ScienceDirect
Applied Soft Computing xxx (2007) xxx–xxx
Applied Soft Computing
www.elsevier.com/locate/asoc

Multicriteria programming in medical diagnosis and treatments

Crina Grosan [a], Ajith Abraham [b,*], Stefan Tigan [c]

[a] Department of Computer Science, Babes-Bolyai University, Cluj-Napoca 3400, Romania
[b] Center of Excellence for Quantifiable Quality of Service (Q2S), Norwegian University of Science and Technology, O.S. Bragstads Plass 2E, N-7491 Trondheim, Norway
[c] Department of Biostatistics and Medical Informatics, Faculty of Medicine, University Iuliu Hatieganu, Cluj-Napoca, Romania

Received 7 October 2006; received in revised form 6 August 2007; accepted 21 October 2007

Abstract

This paper deals with a special case of multicriteria optimization problems. The problems studied come from the medical domain and are of a very important practical relevance. One of the problems refers to the ranking of treatments for the Trigeminal Neuralgia. The second problem refers to a hierarchy of risk factors for Bronchial Asthma. The most common way to deal with a multiobjective optimization problem is to apply Pareto dominance relationship between solutions. But in the cases studied here, a decision cannot be made just by using Pareto dominance. In one of the experiments, all the potential solutions are nondominated (and we need to clearly find a hierarchy of these solutions) and in the second experiment most of the solutions are nondominated between them. We propose a novel multiple criteria procedure and then an evolutionary scheme is applied for solving the problems. Results obtained by the proposed approach in a very simple way are same as the results (or even better) obtained by applying weighted-sum method. The advantage of the proposed technique is that it does not require any additional information about the problem (like weights for each criteria in the case of weighted-sumapproach).

Keywords: Multicriteria analysis; Pareto dominance; Evolutionary algorithm; Weighted sum method; Medical diagnosis; Trigeminal neuralgia; Bronchial asthma

1. Introduction

In a multicriretia optimization problem, instead of one scalar objective function, usually several conflicting and often non-commensurable (i.e. such quantities which have different units) criteria appear in an optimization problem. This situation forces the designer to look for a good compromise solution by considering tradeoffs between the competing criteria. Consequently, the designer must take a decision-maker's role in an interactive design process where typically several optimization problems must be solved. Multicriterion optimization (also known as multiobjective, Pareto, vector optimization) offers a flexible approach for the designer to treat such an overall decision-making problem in a systematic way [32,33].

In scalar optimization, a single optimal solution is often characteristic of the problem, whereas there generally exists a set of Pareto optima as a solution to the multicriteria optimization problem. Mathematically the multicriteria optimization problem can be regarded as solved when the Pareto optimal set has been determined. In practical applications, however, the designer wants only one optimal solution and it is required to introduce some preferences in order to find the best solution among Pareto optima.

Traditionally, problems with several competing criteria were reformulated by using one criterion or scalar objective function and the multicriteria nature of the original problem was more or less hidden. One popular approach is to combine all the criteria into one scalar objective function. Another well known approach is to choose one of the criteria as the objective function and transform the others into constraints. These techniques may look reasonable but they prove to have several shortcomings.

A Pareto optimal set is regarded as the mathematical solution to a multicriterion problem. In continuous problems, the number of Pareto optimal solutions is usually infinite. Only in relatively simple cases the entire Pareto optimal set can be determined analytically. In a typical problem we must be satisfied with obtaining enough Pareto optima to cover the minimal set in the criteria space properly. This computed subset

* Corresponding author.
E-mail addresses: cgrosan@cs.ubbcluj.ro (C. Grosan), ajith.abraham@ieee.org (A. Abraham), stigan@umfcluj.ro (S. Tigan).

1568-4946/$ – see front matter © 2007 Elsevier B.V. All rights reserved.
doi:10.1016/j.asoc.2007.10.014

of Pareto optima could be called as a representative Pareto optimal set and its quality can be judged for example by its ability to cover the whole minimal set evenly. In some problems, however, the cost of generating just one Pareto optimum may become so high that the designer can afford only a few Pareto optimal solutions. Before performing a numerical optimization we must select a generation strategy which guarantees that only Pareto optima are obtained. It is also useful to know which generation techniques cannot reach all Pareto optima and why not.

The most frequently used methods for generating Pareto optima are based on the idea of replacing the multicriterion problem by a parametrized scalar problem. Typically, each parameter combination corresponds to one Pareto optimum and by varying their values it is possible to generate all or the part of the Pareto optimal set.

Several methods have been proposed to deal with multi-objective optimization problems. Among the standard mathematical approaches the most common ones are: Compromise Programming [6], Physical Programming [27], Normal Boundary Intersection (NBI) [7] and the Normal Constraint (NC) [28] methods. There is also a huge amount of work reported on population-based mataheuristics for MOP [34,13–17,9,8,30,37]. Comprehensive surveys can be found in [31,20,29].

There are some particular situations for which Pareto dominance cannot be applied while considering the problem as multiobjective without reducing it to a single objective one. For instance, in the situation in which all solution are nondominated we cannot say that one is better that the other by simply applying Pareto dominance definition.

In this paper, two multiobjective optimization problems are analyzed from the medical domain for which Pareto dominance alone cannot decide which solution is the best. Two cases are considered: in the first case, the problem is to rank a set of treatments applied for Trigeminal Neuralgia by taking into account several criteria. As evident from the considered test data, Pareto dominance cannot be applied in its initial form for classifying these treatments. The result will be that all solutions are nondominated (which, in fact, means that all are equal). In the second case, the problem is to rank a set of risk factors for Bronchial Asthma by taking into account multiple criteria. In this case also, Pareto dominance alone cannot decide which hierarchy is the best (most of the solutions are nondominated between them).

An evolutionary scheme is applied for ranking these treatments. A new dominance concept between two solutions is used. Results obtained are compared with the results obtained by applying weighted-sum method. Data used in experiments represent real data and were analyzed on patients for several years. So, the problems studied are of a very high importance and it is important to find high accurate solutions.

The paper is structured as follows: Section 2 provides details about both problems studied: Trigeminal Neuralgia and Bronchial Asthma. Section 3 describes the effective problem we have to solve in both situations. Section 4 explains the scope of the present research and the motivation of the work done. Section 5 introduces and explains the proposed approach. Section 6 presents the weighted-sum method used for comparing the results of the proposed approach. Section 7 is dedicated to the experiment. Section 8 contains discussions and conclusions of the paper.

2. Medical problems studied

2.1. Case study I—trigeminal neuralgia

Trigeminal neuralgia, also called *tic douloureux*, is a condition that affects the trigeminal nerve (the 5th cranial nerve), one of the largest nerves in the head. The trigeminal nerve is responsible for sending impulses of touch, pain, pressure, and temperature to the brain from the face, jaw, gums, forehead, and around the eyes. Trigeminal neuralgia is characterized by a sudden, severe, electric shock-like or stabbing pain typically felt on one side of the jaw or cheek. The disorder is more common in women than in men and rarely affects anyone younger than 50 years. The pain produced by trigeminal neuralgia is excruciating, perhaps the worst pain know to human beings. The attacks of pain, which generally last several seconds and may be repeated one after the other, may be triggered by talking, brushing teeth, touching the face, chewing, or swallowing. The attacks may come and go throughout the day and last for days, weeks, or months at a time, and then disappear for months or years [1,21,24].

People with trigeminal neuralgia become plagued by intermittent severe pain that interferes with common daily activities such as eating and sleep. They live in fear of unpredictable painful attacks, which leads to sleep deprivation and undereating. The condition can lead to irritability, severe anticipatory anxiety and depression, and life-threatening malnutrition. Suicidal depression is not uncommon. Trigeminal neuralgia most frequently affects women older than 50 years. The disease occurs rarely in those younger than 30 years. Such cases are usually linked to damage from diseases of central nervous system, for example, multiple sclerosis. Medications used to treat trigeminal neuralgia are those used for many other nerve pain syndromes-drugs originally designed to treat seizures. These antiseizure agents suppress excessive nerve tissue activity, which is the cause of the painful syndrome. As a result, they are useful in conditions such as trigeminal neuralgia. Pain specialists use invasive therapy, including nerve blocks, nerve destruction, and nerve decompression techniques, as well as drug therapy to treat trigeminal neuralgia. In some instances, a single injection, or a series of injections, or perhaps one decompressive procedure, will reduce or eliminate the pain and prevent the patient's need for a long course of drug therapy. Injection techniques also can relieve unremitting pain instantly and further confirm the diagnosis.

Using real-time X-rays, doctors can target the anatomical origin of the nerve deep in your skull. Then, with a fine needle, they can inject that source with anesthetic and steroid or they can inject that nerve with a drug used to destroy faulty cells. This procedure can be performed with surprisingly little discomfort (eMedicine).

Medications for trigeminal neuralgia typically includes anticonvulsant such as carbamazepine or phenytoin. Baclofen, clonazepam, gabapentin, and valproic acid may also be effective and may be used in combination to achieve pain relief.

2.2. Case study II—Bronchial Asthma and associated allergies

Asthma (Bronchial Asthma) is an inflammatory disorder of the airways, characterized by periodic attacks of wheezing, shortness of breath, chest tightness, and coughing. Asthma is a disease in which inflammation of the airways causes airflow into and out of the lungs to be restricted. When an asthma attack occurs, the muscles of the Bronchial tree become tight and the lining of the air passages swells, reducing airflow and producing the characteristic wheezing sound. Mucus production is increased [19].

Bronchial Asthma is a public health problem with gradually increasing importance, affecting more than 100 million individuals worldwide and found independently of the level of development of the country. Factors related to lifestyle and the environment form the basis for the increase in the prevalence of the disease [3]. Most people with asthma have periodic wheezing attacks separated by symptom-free periods. Some asthmatics have chronic shortness of breath with episodes of increased shortness of breath. Other asthmatics may have cough as their predominant symptom. Asthma attacks can last minutes to days, and can become dangerous if the airflow becomes severely restricted.

In sensitive individuals, asthma symptoms can be triggered by inhaled allergens (allergy triggers), such as pet dander, dust mites, cockroach allergens, molds, or pollens. Asthma symptoms can also be triggered by respiratory infections, exercise, cold air, tobacco smoke and other pollutants, stress, food, or drug allergies. Aspirin and other non-steroidal anti-inflammatory medications (NSAIDS) provoke asthma in some patients.

Asthma is found in 3–5% of adults and 7–10% of children. Half of the people with asthma develop it before age 10 years, and most develop it before age 30 years. Asthma symptoms can decrease over time, especially in children. Many people with asthma have an individual and/or family history of allergies, such as hay fever (allergic rhinitis) or eczema. Others have no history of allergies or evidence of allergic problems [26]. Recognizing the risk factors is important for the diagnosis and prevention of the disease.

3. Problem formulation

3.1. Trigeminal neuralgia treatment ranking

The problem is to rank treatments illustrated in Table 1 subject to multiple criteria. For the treatment of essential trigeminal neuralgia many methods can be applied. The chronic evolution of the disease, its idiopathic character and the variable response to different treatment methods creates many disputes in the scientific world. The evaluation of the treatment methods from multiple points of view is difficult and has a high degree of subjectivity. The complex and original study with many patients, over the usual number from related studies, can contribute greatly to the evolution of this domain.

Table 1
Treatments applied for Trigeminal Neuralgia

	Treatment
T_1	Infiltrations with streptomycin
T_2	Low level laser therapy
T_3	Treatment by skin graft
T_4	Treatment by sciatic nerve graft
T_5	Treatment by neurectomy

We made a clinical study of the following treatment methods of essential trigeminal neuralgia as described in Table 1.

Remarks.

(i) Among these treatments, neurectomy was considered a mutilating treatment and the other methods were considered conservative.
(ii) The research was performed on 251 patients suffering from essential trigeminal neuralgia and took over 8 years.
(iii) The data used in experiment represent real data and are adapted from [2].

In order to mark out the effects and results of these treatments seven evaluation criteria were considered (see Table 2).

The application of the treatments was based on regular techniques and personal contributions. The evaluation matrix case is presented in Table 3.

Table 2
Criteria considered for treatment efficiency evaluation

	Criterion
C_1	Hospitalization period
C_2	Remission period
C_3	Pain relief
C_4	Decrease in the number of crises
C_5	Decrease in pain level
C_6	Decrease of the pain area
C_7	Decrease in medication

3.2. Bronchial Asthma risk factors ranking

Bronchial Asthma occurs following the interaction between genes and environment, but none of these factors are enough for the disease to express itself. The goal is to establish a hierarchy of the risk factors for BA and the onset of asthma in phenotype. Experiments were done on a group of patients, which have been exposed to risk factors which can be grouped into two categories such as: genetic factors and environmental factors.

Genetic risk factors are:

- Maternal transmission of BA and atopies.
- Mother's BA.
- BA to antecessors.
- All allergies to antecessors (without BA).
- Urticaria to antecessors.

Table 3
Data considered

Criteria	Criterion type	Treatment				
		Infiltrations with streptomycin, T_1	Low level laser therapy, T_2	Treatment by skin graft, T_3	Treatment by sciatic nerve graft, T_4	Treatment by neurectomy, T_5
Hospitalization period, C_1	min	12.143	13.625	15.093	15.417	16.778
Remission period, C_2	min	9.964	10.453	12.07	11.889	12.022
Pain relief, C_3	max	21	18.34	25.2	34.742	18.457
Number of crises, C_4	max	6.667	6.688	11.209	9.75	7.244
Pain level, C_5	max	3.423	3.281	3.558	3.833	3.156
Pain area, C_6	max	0.904	0.937	0.937	0.978	0.848
Medication, C_7	max	364.286	442.188	655.814	586.111	255.556

- Father's BA.
- Eczema to antecessors.
- Rhinitis to antecessors.

Environment risk factors are:
- Life in the city.
- House dust mite.
- House environment (crowd).
- Smoking in the family.
- Traffic pollution.
- Industrial pollution.
- Smoking mother.

The hierarchy has to be established by taking into account six criteria representing BA and the allergies which are present in the phenotype of the patients such as:

- rhinitis,
- conjunctivitis,
- eczema,
- urticaria
- the asthma onset coefficient.

We mention that the evaluation of each criteria of each risk factor has been done by the percentage of the patients who had BA or/and other allergies and have been exposed to one of the risk factors.

Asthma onset coefficient (denoted by CDA) represents an estimate of the risk regarding the BA onset in phenotype. CDA has been established through the average age of the BA onset in patients exposed to a certain (risk) factor (denoted by VDR) and the average age of the BA onset in patients non-exposed to the corresponding (risk) factor (denoted by VDF). CDA is calculated using the following equation:

$$\mathrm{CDA} = \frac{\mathrm{VDF} - \mathrm{VDR}}{\max(\mathrm{VDF}, \mathrm{VDR})}. \quad (1)$$

Asthma onset coefficient CDA has values between -1 and 1. The values of all criteria for the considered risk factor averaged for all the studied patients are given in Table 4.

All objectives are to be maximized. As evident from the data given in Table 4, most of the risk factors are nondominated between them. Only few risk factors are dominated (for instance risk factors 9, 10, 12 and 15). Rest of the factors are all nondominated.

4. Motivation of the present research

The problem of effectively ranking several treatments for Trigeminal Neuralgia and several risk factors for Bronchial Asthma could be formulated as a multiobjective optimization problem due to the number of different criteria which have to be satisfied simultaneously.

The most common approaches of a multiobjective optimization problem use the concept of Pareto dominance as defined below.

Definition 1 (*Pareto dominance*).
Consider a maximization problem. Let x, y be two decision vectors (solutions) from the definition domain.

Solution x dominate y (it also written as $x \succ y$) if and only if the following conditions are fulfilled:

(i) $f_i(x) \geq f_i(y), \forall i = 1, 2, \ldots, n,$
(ii) $\exists j \in \{1, 2, \ldots, n\} : f_j(x) > f_j(y).$

That is, a feasible vector x is Pareto optimal if no feasible vector y can increase some criterion without causing a simultaneous decrease in at least one other criterion.

As evident from the description above, if we are applying the classical Pareto definition in order to obtain a hierarchy of treatments for Trigeminal Neuralgia, all solutions will appear as nondominated. Also, for the second example we cannot establish a clear hierarchy, most of the risk factors being nondominated between them. This way, we cannot say one solution is better than the other. Consequently, any of the existing algorithms dealing with multiobjective problems from a Pareto dominance perspective cannot obtain a desired hierarchy.

One solution is to use one of the traditional mathematical approaches which combine objectives and reduce the problem to a single objective optimization problem. But in this situation, additional information about the problem is required. For instance, every common approach will need details about the importance of each of the criteria. In this situation, a weight

Please cite this article in press as: C. Grosan, et al., Multicriteria programming in medical diagnosis and treatments, Appl. Soft Comput. J. (2007), doi:10.1016/j.asoc.2007.10.014

Table 4
The values of the considered risk factors for the Bronchial Asthma with respect to the considered criteria

	Risk factors	Criteria					
		BA	Conjunctivitis	Rhinitis	Urticaria	Eczema	CDA
1.	House dust mite	81.3	0	21.9	25	12.5	0.218448
2.	Father's BA	84.6	23.1	15.4	15.4	15.4	0.144254
3.	Eczema to antecessors	80	40	40	20	0	−0.22581
4.	Smoking mother	80.6	6.5	9.7	19.4	6.5	0.214712
5.	Traffic pollution	80	3.2	9.7	9.7	12.9	0.338986
6.	House environment (crowd)	73.9	5.8	15.9	23.2	10.1	0.231362
7.	Smoking of other members of the family	71.7	7.5	11.3	17	7.5	0.228511
8.	Industrial pollution	64	8	24	28	8	0.148545
9.	Mother's BA	77.3	0	4.5	9.1	0	0.169509
10.	BA to antecessors	66.7	2.4	12.2	22	6.1	0.087415
11.	Life in the city	65.6	6	15.8	22.6	7.5	0.02771
12.	Maternal transmission of BA and atopies	67.3	0	12.7	16.4	7.3	−0.01284
13.	Rhinitis to antecessors	65	6.7	18.3	15	8.3	−0.19996
14.	All allergies to antecessors (without BA)	60.4	4.4	16.5	17.6	5.5	−0.16459
15.	Urticaria to antecessors	53.2	3.2	11.3	21	3.2	−0.19033

(i.e. a real number between 0 and 1) will be assigned to each criterion. This weight represents the importance (or the percentage) of that criteria between all criteria considered (sum of all these weights is equal to 1).

But in the case analyzed in this paper, all criteria are important; these criteria are direct consequences of a treatment applied in the case od Trigeminal Neuralgia and symptoms of the Bronchial Asthma in the second case studied. So, finding a weight for each criterion is an extra task and can be sometimes difficult to assign.

5. Proposed evolutionary algorithm approach

As mentioned in Introduction of the paper, an Evolutionary Algorithm (EA) [12,18,38] is applied for solving the problems. A special way is used to initialize the population based on some existing information about the units which must be ranked (treatments for Trigeminal Neuralgia and risk factors for Bronchial Asthma, respectively). The evolutionary scheme used here is divided into several steps as presented below.

5.1. Population initialization

For initializing the population in a way which will help in finding the final solution individuals are generated randomly. Each chromosome is represented as a string whose length is equal to the number of units which must be ranked (for instance, treatments in the case of Trigeminal Neuralgia and risk factors for Bronchial Asthma). Instead of filling the positions in the chromosomes with random generated values between 1 and the number of units, a procedure is followed as described below:

(1) Using Pareto dominance, all the nondominated units (treatments and risk factors, respectively) are kept in a separate set (and not considered in the initial set anymore). Let us denote this set by S_1 and the size of this set by s_1. Therefore, first s_1 positions in the chromosome consists of a permutation of the units (indices) from the set S_1 whose ordering is randomly generated.
(2) The procedure described above is repeated until all the levels of nondominated units are selected.

This means, from the remaining units, the nondominated solutions are again selected. These units are nondominated only in respect with the current content of the units set. This new obtained set is denoted by S_2 and the size of this set by s_2.

The minimum number of such levels can be 1 (which means all the solutions are nondominated) and can be maximum the size of the units set.

All the units, which were previously removed from the initial set will dominate these units. Consequently, chromosome positions between s_1+1 and s_2 will consist of random permutations of the units (indices) which are dominated by a single other unit (and are the units belonging to the set S_2, positions between s_2+1 and s_3 will consist of permutations of

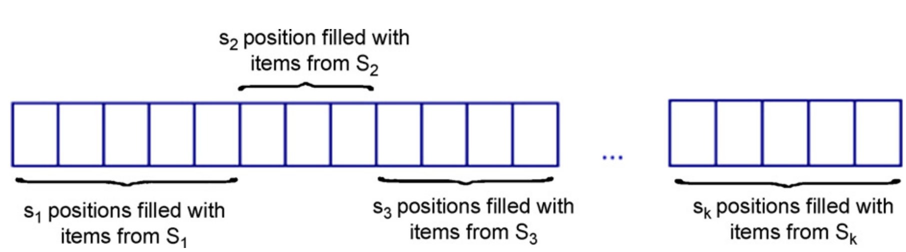
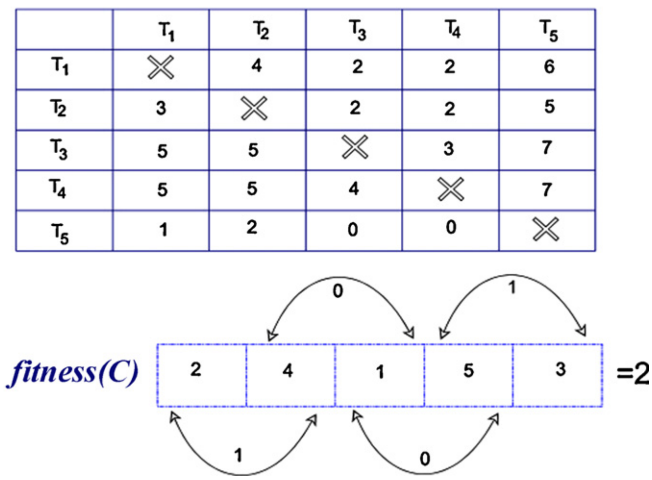


Fig. 1. Example of a chromosome having k levels of dominance.



	T_1	T_2	T_3	T_4	T_5
T_1	✕	4	2	2	6
T_2	3	✕	2	2	5
T_3	5	5	✕	3	7
T_4	5	5	4	✕	7
T_5	1	2	0	0	✕

Fig. 2. Example of fitness function calculation.

the units which are dominated by 2 units (the units from the set S_3, and so on. A graphical example of a chromosome is depicted in Fig. 1. A chromosome is composed of as many segments as the number of levels of dominance, each segment having a different number of genes.

5.2. Fitness function

From the initialization of a chromosome, it is obvious that one gene (which represents an item in our examples, i.e. a treatment in the first case and a risk factor in the second case) cannot be dominated by a successive gene. Two consecutive genes can represent either nondominated items or the second one is dominated by the first one. For establishing a hierarchy when all the items are nondominated and from a multiobjective perspective, the fitness of a chromosome is computed as described in Algorithm 1.

Algorithm 1. Fitness function calculation

Set the value of fitness function to 0.

For each pair of genes $(i, i+1)$ the number of objectives for which i is better than $i+1$ is calculated.

If this number is [is] less than $\frac{\text{number of objectives}}{2}$ (in the case the number of objectives is an even number) or it is less than integer portion of $\frac{\text{number of objectives}}{2} + 1$ (in the case the number of objectives is an odd number) then the value of objective function is increased by 1.

The fitness function will reflect the number of items (treatments, risk factors) which are not correctly arranged with respect to the number of objectives in which one is better than the other.

As depicted in Fig. 1, we consider as example the first case studied in this paper: the Trigeminal Neuralgia treatments. We consider there a chromosome whose genes are (2, 4, 1, 5, 3), which represents the order in which treatments are arranged. Let us use this chromosome as an example and show how the fitness will be calculated in this case. As evident from the table presented in Fig. 2, treatment 2 is better than treatment 4 with respect with two objectives (out of seven). Which means, order must be (4, 2) and not (2, 4). Therefore, the fitness value will increase by 1. Treatment 4 is better than treatment 1 for five of the seven objectives. This means that the order (4, 1) is correct. Treatment 1 is better than treatment 5 for six of the objectives. Again, the pair (5, 1) is correctly arranged. Treatment 5 is not better than treatment 3 for any of the objectives. Means, the order (5, 3) is not correct and fitness will again increase by one. Finally the value of fitness function is equal to 2. Our objective is to obtain the value 0 for the fitness function.

5.3. Evolutionary algorithm

The evolutionary scheme adopted here is very much similar to a classical evolutionary algorithm which uses only mutation as genetic operator. Each chromosome from the population are affected by mutation. Mutation operator works in the following way:

(1) Two genes are randomly chosen from each segment of the chromosome.
(2) The values corresponding to these genes are exchanged between them.

It is to be noted that a gene from a segment of dominance can be only exchanged with another gene from the same segment. Exchanges between genes belonging to different segments are not allowed (see Fig. 3).

The parent and offspring are directly compared. The one with a smaller fitness will be kept into the population of the new generation.

Algorithm 2. The pseudo code of the proposed evolutionary scheme

Step 1. Initialize population following the rules described in the Population Initialization section.

Repeat

Step 2. Compute the fitness (quality) of all individuals.

Step 3. Mutate each solution from the population.

If fitness(parent) < fitness(offspring)
keep the parent for the next generation
else if fitness(offspring) < fitness(parent)
keep the offspring for the next generation
else pick at random between parent and offspring for the next generation.

Until a given number of generations is reached.

Step 4. Print all the individuals with fitness 0.

The pseudo code of the proposed approach is briefly presented in Algorithm 2.

6. Weighted-sum approach

The weighted-sum method is a traditional, popular method that parametrically changes the weights among objective functions to obtain the Pareto front [23].

Let us consider we have the objective functions $f_1, f_2, \ldots, f_n$. This method takes each objective function and multiplies it by a fraction of one, the "weighting coefficient" which is represented by w_i. The modified functions are then added together to obtain a single cost function, which can easily be solved using any method which can be applied for single objective optimization.

Mathematically, the new function is written as:

$$\sum_{i=1}^{n} w_i f_i, \quad \text{where } 0 \leq w_i \leq 1 \text{ and } \sum_{i=1}^{n} w_i = 1.$$

The initial work on the weighted-sum method was done around 1963 by Zadeh [35]. The method is simple to understand and easy to implement. The weight itself reflects the relative importance (preference) among the objective functions under consideration. There are several disadvantages of this technique:

- the user always has to specify the weights values for functions and sometimes this will not have any relationship to the importance of objectives;
- non-convex parts of the Pareto set cannot be obtained by minimizing convex combinations of the objectives;
- a single solution is obtained at one time. If we are interested in obtaining a set of feasible solutions, the algorithm has to be run several times. This also, is not a warranty that the solutions obtained in different runs are different.

7. Experiment results and discussions

The proposed approach is applied for both medical problems: Trigeminal Neuralgia treatments ranking and Bronchial Asthma risk factors ranking. Results obtained by the proposed approach are compared with the results obtained by applying weighted-sum approach.

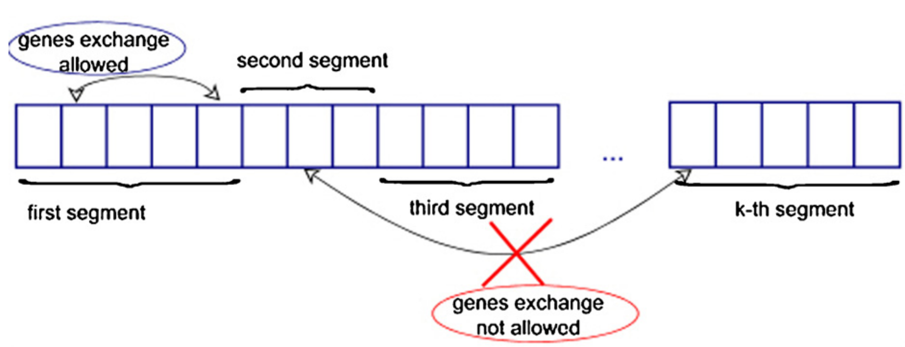


Fig. 3. Example of mutation rules.

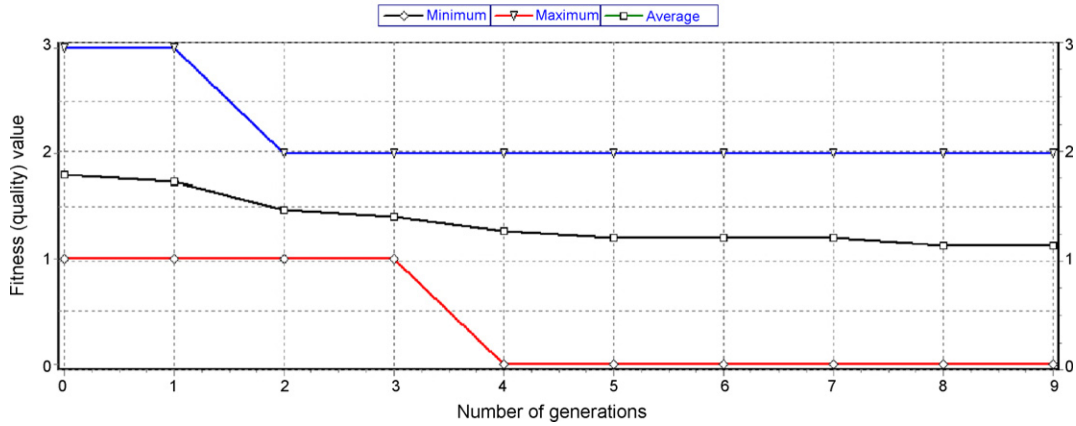


Fig. 4. Evolution of the fitness function for the Trigeminal Neuralgia case study: minimum, maximum and average.

7.1. The case of trigeminal neuralgia

7.1.1. Proposed approach evaluation

The parameters used by the evolutionary approach for the Trigeminal Neuralgia case study are:

- Population size: 20.
- Number of generations: 10.

The hierarchy of treatments efficiency obtained is: T_4, T_3, T_1, T_2, T_5.

An evolution of the fitness function can be analyzed in Fig. 4. The minimum, maximum and average fitness value is depicted for each iteration.

7.1.2. Weighted-sum approach evaluation

As evident from Table 3, first two objectives have to be minimized and last 5 objectives have to be maximized. Weighted-sum approach considers all objectives as having same optimization type (minimization or maximization). For this purpose we consider $-f_1$ and $-f_2$ instead of f_1 and f_2. This way all objectives have to be maximized.

In order to apply weighted-sum method, a weight has to be specified for each criterion. For the seven studied criteria we established specific values within the interval 0.02–0.54. For the hospitalization period and for the remission period, the values were more relevant as they decreased. For the other evaluated parameters, higher values expressed a good efficiency of the evaluated treatment method. Empirical results obtained by applying weighted-sum approach are presented in Table 5.

As evident from Table 5, the ranking of the above treatments in decreasing order of its efficiency obtained by applying weighted-sum approach is: T_4 (Sciatic nerve graft), T_3 (Skin graft), T_1 (Streptomycin), T_2 (Laser) and T_5 (Neurectomy).

7.2. The case of Bronchial Asthma

7.2.1. Proposed approach evaluation

The parameters used by the evolutionary approach for the Bronchial Asthma case study are:

- Population size: 100.
- Number of generations: 100.

Several hierarchies of risk factors are obtained. All the solutions are nondominated between them. Some of the solutions obtained in the final generation are presented in Table 6.

The evolution of the fitness function (performance measure) can be analyzed using Fig. 5. The minimum, maximum and average fitness values are depicted for each iteration.

7.2.2. Weighted-sum method evaluation

Results obtained by the weighted-sum method for ranking the risk factors for Bronchial Asthma are taken from [11]. The weight of each criterion has been evaluated following its frequency in the patient phenotype. The frequencies of the allergies of the patient have been mentioned. BA was evaluated

Table 5
Results obtained by applying weighted-sum approach

Treatment	Criteria							Weighted-sum
	C_1	C_2	C_3	C_4	C_5	C_6	C_7	
T_1	12.143	9.964	21.0	6.667	3.423	0.904	364.286	18.21691
T_2	13.635	10.453	18.34	6.688	3.281	0.922	442.188	18.16829
T_3	15.093	12.07	25.2	11.209	3.558	0.937	655.814	26.34107
T_4	15.417	11.889	34.742	9.75	3.833	0.978	586.111	30.01671
T_5	16.778	12.022	18.457	7.244	3.156	0.848	255.556	14.17278
Weights	0.08	0.06	0.54	0.08	0.17	0.05	0.02	

Table 6
Example of nondominated solutions obtained by the evolutionary approach for the Bronchial Asthma case study

1.	2 11 4 3 8 1 7 5 6 13 14 12 10 15 9
2.	8 7 14 5 4 2 1 11 3 13 4 10 12 15 9
3.	2 1 7 11 13 4 3 5 6 8 14 12 10 15 9
4.	1 8 3 2 7 14 5 6 4 13 11 12 10 15 9
5.	7 13 4 14 5 1 8 6 2 11 3 12 10 15 9
6.	8 1 4 3 2 5 6 7 13 11 14 12 10 15 9
7.	14 5 1 2 8 6 11 3 7 13 4 12 10 15 9
8.	6 8 12 13 11 5 7 4 2 14 12 10 15 9
9.	1 2 6 7 13 14 5 8 3 11 4 10 12 15 9
10.	3 6 2 1 8 13 14 5 7 11 4 19 12 15 9
11.	1 7 14 5 6 4 3 2 8 11 13 10 12 15 9
12.	1 8 6 2 14 5 13 4 3 7 11 12 10 15 9
13.	6 13 14 5 8 1 2 7 4 11 3 10 12 15 9
14.	1 6 2 14 5 7 13 4 3 8 11 10 12 15 9

Each solution represents the order in which risk factors are ranked.

after the frequency of the patients with BA alone. The sum of frequencies is 114, 3% which represents 100 points from the total weight. Thus, has been set the weight of each criterion. BA and BA onset have been initially evaluated together, with a total weight of 58 points, and then they have been evaluated after the importance considered to represents the BA onset in the evaluation of the risk disease and have been granted 8 points. Results obtained by applying weighted-sum method are presented in Table 7.

7.2.3. Results analysis

As evident from the first experiment, both algorithms obtained same hierarchy for the treatments. The advantage of the evolutionary approach is more evident for the second case study which was more difficult. Some important aspects of the proposed evolutionary approach are depicted below:

(1) Several alternative solutions are obtained by the evolutionary approach when compared to a single solution obtained by the weighted-sum approach. Of course, by selecting different values for the weights, multiple solutions can be obtained by the weighted-sum method also, but in different runs. But in this case, weights are important. For instance, a weight whose value was 0.5 (out of 1) or 50 (out of 100) cannot be 0.1 (or 10, respectively). This means there is no rule in establish the importance of objectives. So,

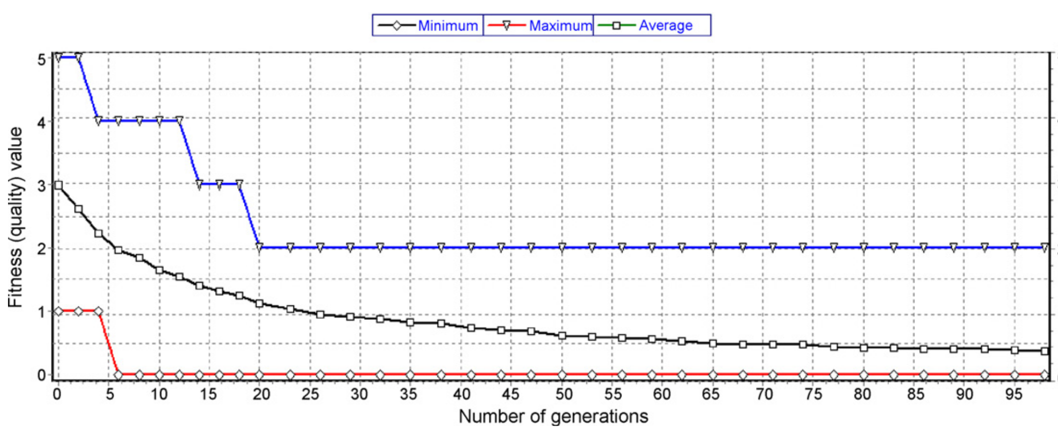


Fig. 5. Evolution of the fitness function for the Bronchial Asthma case study: minimum, maximu and average values.

Table 7
Results obtained by weighted-sum method for the Bronchial Asthma case study

Risk factor	Criteria						Score
	BA	Conjunctivitis	Rhinitis	Urticaria	Eczema	CDA	
House dust mite	81.3	0	21.9	25	12.5	0.22	50.74
Father's BA	84.6	23.1	15.4	15.4	15.4	0.14	50.23
Eczema to antecessors	80	40	40	20	0	−0.2	48.79
Smoking mother	80.6	6.5	9.7	19.4	6.5	0.21	47.61
Traffic pollution	80	3.2	9.7	9.7	12.9	0.34	46.71
House environment (crowd)	73.9	5.8	15.9	23.2	10.1	0.23	46.11
Smoking in the family	71.7	7.5	11.3	17	7.5	0.23	43.12
Industrial pollution	64	8	24	28	8	0.15	42.42
Mother's BA	77.3	0	4.5	9.1	0	0.17	42.32
BA to antecessors	66.7	2.4	12.2	22	6.1	0.09	40.27
Life in the city	65.6	6	15.8	22.6	7.5	0.03	40.05
Maternal transmission of BA/atopy	67.3	0	12.7	16.4	7.3	−0.01	38.75
Rhinitis to antecessors	65	6.7	18.3	15	8.3	−0.2	36.89
All allergies to antecessors (without BA)	60.4	4.4	16.5	17.6	5.5	−0.2	34.87
Urticaria to antecessors	53.2	3.2	11.3	21	3.2	−0.2	30.85
Weights	50	4	13	19	6	8	

Please cite this article in press as: C. Grosan, et al., Multicriteria programming in medical diagnosis and treatments, Appl. Soft Comput. J. (2007), doi:10.1016/j.asoc.2007.10.014

choosing the appropriate weights is not an easy task. For instance, we considered decreasing of pain criteria as being a very important one (weight is 0.54) and medication period (or hospitalization period) as having a less importance (weights are 0.08 and 0.02, respectively). If the pain weight and medication weight are exchanged we cannot have any warranty of the result quality.

(2) As evident from the data given in Table 7, the risk factor 9 is dominated with respect to all objectives by three other risk factors (1, 4 and 5), risk factor 15 is dominated by two risk factors (6 and 8), risk factors 10 and 12 are dominated by a single risk factor (6). This means, in the resulting hierarchy, factor 9 must be on the last position. Factors 15, 10 and 12 are also dominated and must be in one of the last positions. But this is not evident from the hierarchy obtained by the weighted-sum approach. All these domination relations are taken into account by the evolutionary method and several alternatives of risk factors ranking are obtained at the end of the search process.

(3) In the results obtained by the evolutionary approach for the second case study, genetic factors are of a very high importance (as shown in other medical studies such as [5,3,22]). Also, hierarchy obtained by the evolutionary approach shows the same thing.

(4) Experiment results show a very fast convergence of the evolutionary approach.

(5) The evolutionary approach proposed herein is very flexible and can be applied to any problem of this kind. No additional information about the problem are required (like different weights in the case of weighted-sum method).

8. Discussions and conclusions

While referring to the first case study, the Trigeminal Neuralgia treatments ranking, the patients had different responses in time to the same treatment method. This observation can be found also in other studies [25]. The inadequate dosing of medications or treatments can also lead to failure [36].

The essential trigeminal neuralgia is characterized by a cyclic evolution. As the disease evolves, an increase of the active periods is noticed, respectively, an increase of the need of the treatment. Also a resistance to the treatments is noticed. All these show that more methods are needed in the therapeutic arsenal of the essential trigeminal neuralgia and their evaluation can be the method to select the best treatment. More authors say that the choosing of the treatment is a difficult task [4,10]. The clinician must discover the real dimension of the pain and its ties to the psychological level, to be able to include in the treatment the whole suffering of the patient and its real levels.

The recorded results show that a treatment method does not have constant better effects on all criteria than another. This practically means that Pareto dominance will not provide any information about the dominance of one treatment or another. All are classified as equal.

By applying evolutionary algorithms, the ranking of treatments efficiency obtained is similar to the one obtained by applying a standard mathematical approach for multiobjective optimization: weighted sun approach. But the advantage is that we do not require any additional information about the problem while weighted-sum approach involves a weight for each objective. This task can be sometimes difficult to achieve due to the objectives importance.

By combining all objectives in a single objective function (and transforming the multiobjective optimization problem in a single objective one) at one application of the algorithm can be obtained at most one solution. In order to obtain multiple solutions we have to apply the algorithm several times. Even then, we cannot be sure that all solutions are different. Running time required is another disadvantage of the weighted-sum approach. This is the case for our second case study: Bronchial Asthma risk factors ranking. The evolutionary approach obtain several solutions in one run. Also, the dominance concept (which is more than standard Pareto dominance relationship) is playing and important role in the final hierarchy. Both genetic and environmental factors represent a risk for the Bronchial Asthma and their influence differs from a patient to another, from a world region to another, etc. Genetic susceptibility is both context dependent and developmentally regulated, and ignoring the environmental context will miss many important associations and clues to pathogenesis. That's why a right classification of the risk factors is very important in control and prevention of Bronchial Asthma.

References

[1] R.I. Apfelbaum, Trigeminal Neuralgia: Vascular Decompression. Carter and Spetzler—Neurovascular Surgery, Mc Graw Hill International ed., 1995, pp. 1107–1118.
[2] R. Campian, G. Baciut, M. Baciut, S. Tigan, Pain evaluation in essential trigeminal neuralgia of essential trigeminal neuralgia treatments, Applied Medical Informatics, Cluj-Napoca 15 (3–4) (2004) 21–25.
[3] M.R. Cengizlier, E.D. Misirlioglu, Evaluation of risk factors in patients diagnosed with bronchial asthma, Allergol. Immunopathol. (Madr.) 34 (1) (2006) 4–9.
[4] S. Esposito, A. Delitala, P. Bruni, R. Hernandez, G.M. Callovini, Therapeutic protocol in the treatment of trigeminal neuralgia, Appl. Neurophysiol. 48 (1–6) (1985) 271–273.
[5] W. Burke, M. Fesinmeyer, K. Reed, L. Hampson, C. Carlsten, Family history as a predictor of asthma risk, Am. J. Prevent. Med. 24 (2) (2003) 160–169.
[6] W. Chen, M.M. Wiecek, J. Zhang, Quality utility—a compromise programming approach to robust design, J. Mech. Des. 121 (1999) 179–187.
[7] I. Das, On characterizing the 'knee' of the Pareto curve based on normal-boundary intersection, Struct. Optim. 18 (2–3) (1999) 107–115.
[8] K. Deb, Multiobjective Optimization Using Evolutionary Algorithms. Series in Systems and Optimization, John Wiley and Sons, Chichester, England, 2001.
[9] M. Ehrgott, M.M. Wiecek, Mutiobjective programming, in multiple criteria decision analisys: state of the art surveys, in: J. Figueira (Ed.), International Series in Operations Research & Management Science, vol. 78, Springer, New York, 2005.
[10] M.I. Gerasimenko, I.V. Grachev, A.A. Nikitin, A.D. Kalachan, Physical factors in the combined treatment of trigeminal prosopalgias, Stomatologiia 78 (2) (1999) 40–41.
[11] M. Gherman, M. Moldoveanu, S. Tigan, Hierarchy of risk factors in bronchial asthma, Appl. Med. Inf. 14 (1–2) (2004) 35–41.
[12] D.E. Goldberg, Genetic Algorithms in Search, Optimization and Machine Learning, Addison Wesley, Reading, MA, 1989.

[13] C. Grosan, A. Abraham, Evolutionary multiobjective optimization for large scale systems of equations, IEEE Trans. Syst. Man Cyber—Part A (2008), in press.
[14] C. Grosan, A. Abraham, M. Nicoara, Search optimization using hybrid particle sub-swarms and evolutionary algorithms, Int. J. Simul. Syst. Sci. Technol. 6 (10–11) (2005) 60–79.
[15] C. Grosan, M. Oltean, Adaptive Representation for Single Objective Optimization Soft Computing, vol. 9, Springer-Verlag, 2005, pp. 594–605.
[16] C. Grosan, A. Abraham, Modified line search method for optimization, in: First IEEE Asia International Conference on Modeling and Simulation AMS-07, IEEE Computer Society Press, Thailand, 2007, pp. 415–420, ISBN: 0–7695-2845–7.
[17] C. Grosan, Multiobjective adaptive representation evolutionary algorithm (MAREA)—a new evolutionary algorithm for multiobjective optimization, in: Proceedings of 9th World on-line Conference on Soft Computing in Industrial Application, Applied Soft Computing Technologies: The Challenge of Complexity, Advances in Soft Computing, Springer Verlag, Germany, 2006, pp. 113–121.
[18] J. Holland, Adaptation in Natural and Artificial Systems, University of Michigan Press, Ann Arbor, 1975.
[19] http://www.emedicine.com.
[20] J. Jahn, Vector Optimization: Theory, Applications and Extensions, Springer-Verlag, Berlin, 2004.
[21] P.J. Jannetta, Microvascular Decompression of The Trigeminal Nerve for Tic Douloreux. Youmans—Neurological Surgery, vol. 5, fourth ed., Saunders Company, 1996, pp. 3404–3415.
[22] K. Koenig, Families discovering asthma in their high-risk infants and toddlers with severe persistent disease, J. Family Nurs. 12 (1) (2006) 56–79.
[23] I.Y. Kim, O.L. de Weck, Adaptive weighted-sum method for bi-objective optimization: Pareto front generation, Struct. Multidiscip. Optim. 29 (2005) 149–158.
[24] A. Kondo, Follow-up results in microvascular decompression in trigeminal neuralgia and hemifacial spasm, Neurosurgery 40 (1997) 46–52.
[25] K.H. Lee, Facial pain: trigeminal neuralgia, Ann. Acad. Med. Singapore 22 (2) (1993) 193–196.
[26] MedlinePlus Medical Encyclopedia. http://www.nlm.nih.gov/medlineplus/ency/article/000141.htm.
[27] A. Messac, C.A. Mattson, Generating well-distributed sets of Pareto points for engineering design using physical programming, Optim. Eng. 3 (2002) 431–450.
[28] A. Messac, A. Ismail-Yahaya, C.A. Mattson, The normalized normal constraint method for generating the Pareto frontier, Struct. Multidiscip. Optim. 25 (2) (2003) 86–98.
[29] K.M. Miettinen, Nonlinear Multiobjective Optimization, Kluwer Academic Publishers, Norwell, 1999.
[30] M.G.C. Resende, J.P. de Sousa, Metaheuristics: Computer Decision-Making, Kluwer Academic Publishers, The Nederlands, 2004.
[31] S. Ruzika, M.M. Wiecek, Approximation methods in multiobjective programming, J. Optim. Theor. Appl. 126 (3) (2005) 473–501.
[32] W. Stadler, A survey of multicriteria optimization, or the vector maximum problem, J. Optim. Theor. Appl. 29 (1979) 1–52.
[33] R.E. Steuer, Multiple Criteria Optimization: Theory Computation and Application, Wiley, New York, 1986.
[34] A. Tiwari, R. Roy, G. Jared, O. Munaux, Evolutionary-based techniques for real-life optimisation, Dev. Test. Appl. Soft Comput. 1 (4) (2002) 301–329.
[35] L. Zadeh, Optimality and non-scalar-valued performance criteria, IEEE Trans. Autom. Control 8 (1963) 59–60.
[36] J.M. Zakrzewska, P.N. Patsalos, Drugs used in the management of the trigeminal neuralgia, Oral Surg Oral Med Oral Pathol. 74 (4) (1992) 439–450.
[37] Z. Zhang, Immune optimization algorithm for constrained nonlinear multiobjective optimization problems, Appl. Soft Comput. 7 (3) (2007) 840–857.
[38] C. Grosan, A. Abraham, R. Campian, S. Tigan, Evolution Strategies for Ranking Several Trigeminal Neuralgia Treatments, Appl. Med. Inf. 17 (3–4) (2005) 72–78.