The Use of Fuzzy Measures in Pain Relief Control

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Abstract: *Many people suffer from a continuous strong pain which is caused solely by the malfunction of the pain mechanism itself. One way to ease their pain is to electrically stimulate the spinal cord. Since the equations of pain are not known, we must use heuristic methods to find the optimal pain relief stimulation. In this paper, we show how fuzzy measures and similar nonlinear models can be used in pain relief control: they can be used to determine the parameters of the model which describes the dependence of the pain relief on the applied stimulation. Thus, fuzzy measures lead to the determination, for a given pain distribution, of the optimal pain relief stimulation.*

Keywords *Fuzzy measure, Pain relief*

1 Pain Relief is a Serious Problem

Pain is unpleasant, but it serves an important goal: it signals to the brain that something is wrong with a certain part of the body. Unfortunately, the pain-generating mechanism itself is as prone to mis-perform as any other physiological mechanism in our bodies. Ideally, we should get a pain signal in the presence of damage, and no pain signal if there is no damage. If the pain mechanics mis-performs, we can get one of the two errors:

- there is a damage, but no pain is felt;
- there is no serious damage, but a severe pain is felt.

Situations of the first type mainly require caution, frequent tests, etc.; in other words, these situations are manageable.

Situations of the second type are much more serious: they lead to a continuous strong pain (*chronic pain*) that is not an indication of any physiological damage. Chronic pain is a serious health problem that, according to some estimates (see, e.g., [4–6,10]), affects up to 10% of the world population, including more than 25 million of people in the United States only. Chronic pain may not be perceived as such a threat as cancer or heart diseases because, unlike these diseases, it does not kill. However (according to the above-mentioned estimates) chronic pain disables more people than cancer or heart disease, and costs the US economy more than $90 billion per year in medical costs, disability payments, and lost productivity.

To ease the suffering of the patients suffering from the chronic pain, it is desirable to stop the pain signals from being received by the brain. This is a very difficult task because, although we can monitor the signals coming through the neurons, the existing technology is not capable of differentiating between neuron impulses that correspond to pain and other types of neural impulses. Since the physiology of pain is still at its infancy, we need some indirect *heuristic* methods to get rid of the pain.

In the following two sections, we will describe a brief history of such methods (for a detailed history, see, e.g., [4–6,10]).

2 Easing Chronic Pain: a Brief History

Let us briefly describe the history of the suse of electrical signals in pain releif.

Since pain signals are simply electric signals, it is natural to use electricity to treat chronic pain.

The use of electricity to treat chronic pain has its roots in the ancient world: Roman physicians prescribed the use of "electric fish" in the treatment of their first century patients. The modern use of electricity to treat pain began in the 1750's, when European researchers experimented with newly-invented mechanical devices capable of producing static electricity. The invention of the electrochemical battery in 1800 led to improved treatments. By 1826 guidelines for the use of direct current in medical treatment had been published. The use of electrostimulation gradually diminished after 1900, when the

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credibility of the treatment was undermined by unsupported claims of earlier researchers.

3 Easing Chronic Pain: the Idea of Spinal Cord Stimulation (SCS) and Its Current Achievements

The problem of easing chronic pain is made somewhat easier by the fact that all the pain signals, no matter where they originate, go through the *spinal cord* before they reach the brain. So, the idea is to surgically insert electrodes attached to different points on the spine, and then apply a trial-and-error method to find the combination of signals that would eliminate or at least ease this pain.

This idea was known for quite some time, but it was only implemented in the 1960's, because the implementation of this idea is not easy at all: we want to target the pain in a certain area and so, we need to find the place on the spine that corresponds to this very area of the body. This place is usually very small and difficult to find.

The first clinical trials of this idea were not always successful: Following the *gate control* theory, by Melzack and Wall in 1965 [9], Shealy *et al.*, and Wall and Sweet published first clinical reports of pain relief by direct spinal cord stimulation in 1967 [11–13]. Many inappropriate patients were subsequently implanted and large numbers of failures resulted.

During the 1970's significant improvements in technology occurred, resulting in greater success. In 1973, Cook published favorable responses in multiple sclerosis patients. Shimoji developed a catheter type electrode in 1974. Waltz developed a laminotomy type electrode for clinical applications. In 1979 quadrapolar electrode catheters were introduced.

In the 1980's technology continued to advance, as did the types of conditions identified for treatment using SCS. Surgical instruments were refined and better radiological imaging equipment led to the procedure becoming more widely used. The first multi-programmable electronics were introduced in 1980, and totally implantable neural stimulator systems were introduced in 1981. Eight-channel multiprogrammable electronics and the first eight-electrode catheter were developed in 1986. In 1988 the non-invasive programmable implantable pulse generator that also had radio frequency capabilities was introduced.

In the 90's as patients with more complex conditions were identified, use of multi-lead electrode arrays was adopted. As a result, implantable programmable pulse generators, implantable radio frequency receivers, and more sophisticated objective patient screening methods have led to improved outcomes (for detailed surveys, see, e.g., [4–6,10]).

4 Easing Chronic Pain by Spinal Cord Stimulation: Main Problem

In spite of the successes of Spinal Cord Stimulation in easing chronic pain, there are still several unsolved problems:

- First, there are, currently, only a few medical doctors knowledgeable and qualified enough to perform these procedures. It is desirable to use the knowledge of these doctors for creating a software helping tool that will help other doctors apply similar techniques. One of the possibilities is to design a computer-based simulator to help the doctors learn this technique.

- Second, the current adjustment procedures take too long. In the academic environment, where a doctor can spend dozens of hours with each patient, the success rate is very high: in the majority of cases, there is a drastic pain relief. However, in the clinical environment, we cannot afford to spend that much time with each patient. It is, therefore desirable to design a special computer-based tool that would speed up this adjustment phase. Since each adjustment requires a feedback from the patient, we need, therefore, a computer-based simulation tool that would help the patient to speed up the learning process.

- Finally, although the existing combinations of signals help to ease the pain in the majority of the patients, with some patients, there is no drastic pain relief, and even if there is, it is desirable to eliminate the pain altogether. For that purpose, medical engineers are currently developing a new generation of implanted tools that would enable us to drastically increase the variety of different signals sent to the spine and thus, hopefully, increase the possibility that some combination of these signals will help every patient. But with this variety comes a problem: we cannot any longer test all possible combinations of these signals (there are more than 40 million possible combinations), so we need to design an intelligent method of finding the best combination without going through all of them.

5 What We Are Planning to Do

In our previous papers [1–3], we have made some advance towards solving this problem by using different approaches from mathematical optimization and Artificial Intelligence. In particular, since one of the main problems is the fact that pain is a very subjective feeling, difficult to measure, it is very natural to use fuzzy techniques to get numerical measures of this subjective feeling.

In this paper, we show that a further progress can be obtained if we use the idea of a *fuzzy measure*.

6 What is a Fuzzy Measure and Why This Notion May Be Useful in Pain Relief

6.1 Traditional Mathematical Notion of a Measure

In mathematics, a *measure* is usually defined as an *additive* function on a class of sets. To be more precise, we have a *universal set* U, and a class $\mathcal{A}$ of subsets of this set; a measure is a function μ which maps every set $A \in \mathcal{A}$ into a real number in such a way that if A and A' have no common elements, then $\mu(A \cup A') = \mu(A) + \mu(A')$ (and also if sets A_i are mutually disjoint, then $\mu(\cup A_i) = \sum \mu(A_i)$).

Usually, only *non-negative* measures are considered, i.e., measures μ whose values $\mu(A)$ are non-negative for all sets A.

Measures are used in many applications. There are two main areas of application of measures:

- *geometric* measures, where $\mu(A)$ is an area (volume, etc.) of a geometric domain A; these measured form the basis of spatial *integration*; and
- *probabilistic* measures, where U is the set of all possible *situations*, subsets $A \subseteq U$ correspond to *events* (i.e., properties of situations), and $\mu(A)$ is equal to the probability of the event A.

In Artificial Intelligence, geometric measures are rare, and the main use of measures is via probability measures.

The notion of a measure plays an extremely important role in mathematical foundations of probability: actually, in mathematics, a probabilistic measure is defined as a measure μ for which $\mu(U) = 1$ (this definition was invented by A. Kolmogorov in 1933 who showed that it leads to an exact mathematical foundation of all formulas and results of probability calculus).

6.2 From Standard Mathematical Measures to Fuzzy Measures

Fuzzy methodology started with an observation that not all types of uncertainty can be easily described by probabilities. Since probability theory exists for several centuries and has many useful notions, naturally many researchers tried to adjust notions developed in probability theory to a fuzzy case. In particular, since the notion of a measure is extremely important in probability theory, researchers tried to find fuzzy analogues of this notion.

In fuzzy methodology, there is a natural analogue of a probability $P(A)$ of the event A: the degree $\mathrm{Poss}(A)$ to which this event is possible. From the mathematical viewpoint, the main difference between probability measures and the possibility measures is that possibility measures are not necessarily additive.

As a result, the mathematical notion of a fuzzy measure was introduced: as a mapping (not necessarily additive) from sets to real numbers.

This definition is very general, so it does not allow for a general useful mathematical theory; however, due to its closeness to the description of fuzzy uncertainty, this notion proved to be useful in many applications of fuzzy techniques (see, e.g., [7]).

6.3 From Fuzzy Measures to Fuzzy Integrals

As we have mentioned, standard (additive) measures are used in the definition of integration: both in the geometric integration and in the probabilistic integration (computation of the average). An integral $I(f) = \int_a^b f(x)\,\mathrm{d}x$ can be viewed as a mapping which maps functions f into real numbers $I(f)$. Since the measure is additive, the corresponding functions are linear.

For fuzzy measures, it is also natural to define fuzzy analogues of the classical integral. For example, an *average* is an attempt to characterize a random variable by a single number; similarly, we often need to characterize a fuzzy variable by a single crisp number, so we need the notion of a *defuzzification*. Since fuzzy measures are not necessarily additive, the resulting mappings from functions to real numbers are not necessarily linear. For example:

- In a linear mapping, $I(2f) = 2I(f)$, i.e., if we double all the values of the function, then its integral increases.
- However, e.g., for defuzzification, if we double our degree of belief in each possible value x, this may simply mean that we started to use a new scale to represent our degrees of belief, and in reality, our beliefs did not change. In this interpretation, there is no reason to change the defuzzification value at all, i.e., $I(2f)$ should be equal to $I(f)$.

There are many different generalization of the notion of integral to fuzzy cases; the most general would be to define a "fuzzy integral" as a mapping (not necessarily linear) from functions to real numbers.

6.4 Fuzzy Measure and Generalized Fuzzy Integral in Pain Relief Applications

In order to properly relieve pain by using spinal cord stimulation, we must know which points to activate and how big the activation signals need to be.

Since we do not know the exact nature of electric signals traveling along the spinal cord, it is extremely dangerous to send large signals: it is known that, since the muscle activation is also triggered by similar electric signals, large signals can cause uncomfortable, painful and even dangerous involuntary muscle contractions. On the other hand, to prevent a living being from reacting to too many unnecessary signals, a body works in such a way that signals which are too weak are not felt at all. As a result, there is a reasonably narrow window of opportunity starting from the barely feel-able signal to the dangerous level of muscle contraction.

It is very difficult to get into this window, and it is even more difficult to find the "optimal" signal within this window so that:

- we eliminate all the pain and at the same time
- avoid the unnecessary and unpleasant activations of body areas which are not affected by pain.

To be able to automatically solve the corresponding optimization problem, we must have a formal description of how a body reacts to different signals. Of course, different people react differently, so we cannot have a single description, we must have a *parameterized* description, so that we will be able to adjust to any patient by experimentally finding the values of the corresponding parameters. Since determining each parameter requires time-consuming costly experiments, we would like to have as few parameters as possible.

Before we start answering the question of *how* to describe the body's reaction in precise mathematical terms, let us first find out what type of mathematical object we are looking for.

The reaction of the body to different signals can be found out if we know how each body area reacts to these signals. So, it is sufficient to describe the reaction of a single body area to different signals.

A signal x can be described by specifying the amount of activation $x(t)$ applied to each activation point t. Since people cannot meaningfully calibrate their feelings, for each signal x, the only thing that a patient can tell for sure is whether there is a feeling or not. So, for each signal x, the reaction in a given body part is equal to 1 (there is a reaction), or to 0 (no reaction). In other words, the reaction that we want to describe is a mapping R which maps every signal (function) $x(t)$ into 0 or 1.

This mapping R is not linear: e.g., if we take the signal which causes reaction, i.e., for which $R(x) = 1$, then, no matter whether $R(x/2) = 0$ or $R(x/2) = 1$, we cannot have $R(x) = 2R(x/2)$. Thus, this mapping is not a regular integral, but a generalized fuzzy integral.

Similarly, if we are only interested in knowing which activation points to activate, i.e., if we a signal can be characterized only by the *set* of points to which activation is applied, then the reaction function becomes a fuzzy measure.

Our goal is therefore to determine the corresponding fuzzy measure (or the corresponding generalized fuzzy integral) by performing as few experiments as possible.

7 Fuzzy Measures and Generalized Fuzzy Integrals Relevant for Pain Relief, and How They Can Be Used in Pain Relief Control

7.1 Fuzzy Measures and Generalized Fuzzy Integrals Relevant for Pain Relief: Neural-Type

Sensors on a human body are extremely sensitive:

- It is well know that astronauts in space can be trained to see tiny details of earth events which only the newest most sophisticated optimal cameras can capture.
- A trained human nose can test faint smells (i.e., microscopic quantities of certain chemicals) which cannot sensors often cannot detect.

In both cases, the training does not change the sensor itself, it changes the way we process the information from this sensor. In other words, in the original un-trained state, nose sensors detect the faint smells, and the reason why an un-trained person does not recognize them is because the processing neurons suppress the signals coming from the nose.

Similarly, it can be shown that the neurons do react to even a very weak electric stimulation, and the reason why the human body does not react to such weak electric activation is that the processing neurons suppress this reaction before it reaches our conscience.

In the first approximation, we know how data processing is done in a neuron – this description is implemented in modern artificial neurons which form the basis of successful artificial neural networks. Therefore, in the first approximation, we will assume that the signals $x(t)$ applied to different activation points get processed by a processing neuron, and this explains the observed reaction $R(x)$.

The (simplified) description of how a neuron processes data is as follows: signals $x_1, \ldots, x_n$ come to the processing neuron via different inputs; these signals are combined together, with different weights, into a weighted linear combination

$$y = w_1 \cdot x_1 + \ldots + w_n \cdot x_n;$$

and then this combined signal passes through a threshold-type function $s(y)$ whose output is close to 0 for y much smaller than a certain positive threshold y_0 and $s(y) = 1$ for signals which are much larger than y_0.

In artificial neural networks, the threshold function usually takes the form $s(y) = 1/(1 + \exp(-y))$. However, in our case, we want to explain the reaction mapping $R(x)$ which only takes values 0 or 1.

So, we want to avoid activations functions which can take values intermediate between 0 and 1. Therefore, we consider the activation step-function $s(y) = 0$ for $y < y_0$ and $s(y) = 1$ for $y \geq y_0$. For this activation function, the output $z = s(y)$ of a neuron takes the following form: $z = 0$ if $w_1 \cdot x_1 + \ldots + w_n \cdot x_n < y_0$, and $z = 1$ otherwise.

This formula which describes this neuron's output contains $n+1$ parameters $w_1, \ldots, w_n, y_0$. However, it can be further simplified: if we divide both sides of the corresponding inequality by the positive value y_0 and denote w_i/y_o by c_i, we can conclude that $z = 0$ if $c_1 \cdot x_1 + \ldots + c_n \cdot x_n < 1$, and $z = 1$ otherwise.

Thus, for pain relief control, we are interested in considering only generalized fuzzy integrals which can be described by neural-type formulas: $R(x) = 1$ if $\sum_t c_t \cdot x(t) < 1$ and $R(x) = 1$ otherwise.

7.2 How to Use Neural-Type Fuzzy Measures and Generalized Fuzzy Integrals in Pain Relief Control

It is possible. In order to determine the appropriate relief control, we must experimentally determine the values of the coefficients c_i. The first natural question is whether it is at all possible to determine these coefficients. This equation has been formulated in a more general situation and the answer is, in general, "yes" (see, e.g., [8]).

So, the remaining (and from the practical viewpoint, the most important) question is *how* can we determine these coefficients.

Simplest case – when there is only one activation point – is easy. If we had only one activation point which affects a given body area, then the activation signal would simply be one number, and the activation function $R(x)$ would be easy to describe: it is 0 for $x < x_0$ and 1 for $x \geq x_0$, where x_0 is the (unknown) threshold. In this case, to describe the activation function, it is sufficient to describe the threshold value x_0. To determine this value x_0, we can cautiously enlarge x until a patient starts feeling the signal.

Let us reduce – as much as possible – the entire problem to this simplest case. Since the case of a single activation point is so easy to solve, it is desirable to try to separate the effects of different activation points, and to determine each of the coefficients c_t by activating only the corresponding activation point.

If we try to implement this strategy, we arrive at the following algorithm:

Algorithm for determining the values c_t^a for all body areas a: first stage. So, we start with experiments in which only one activation point is activated. For each activation point t, we slowly increase the activation level $x(t)$, until we get a feeling in one of the body areas a. According to the description of the reaction function, for this one-point signal, we get a feeling in the area a when the product $c_t^a \cdot x(t)$ grows to the level 1. Thus, the corresponding coefficient c_t^a can be determined as $1/x(t)$, where $x(t)$ is the first value of the signal for which a patient started feeling something in this body area.

After that, we continue increasing the signal, and hopefully, we will be able to determine several more coefficients c_t^a; the increase continues until a patient starts getting uncomfortable feeling in one of the areas. The repetition of this experiment for all activation points constitutes the first stage of our algorithm.

It is known that for each body area a, there is an activation point t which affects this particular body area in the largest possible way. Therefore, when we activate only this point, we reach a feeling level in a without exceeding the dangerous level in any other body areas. Thus, we will be able to determine the value of the corresponding coefficient c_t^a. So, as a result of the first stage, for each body area, we know at least one coefficient c_t^a.

We can use the same experiments to also determine the level of discomfort. Namely, we can assume that the discomfort in a body area a is characterized by a larger threshold $y_a > 1$. So, when we apply a signal to the activation point t and at some level x, a patient starts feeling discomfort in an area a, we can therefore determine the discomfort level of this area as $y_a = c_t^a \cdot x$. Since the feeling level is below the discomfort level, we have already determined the value c_t^a.

Algorithm for determining the values c_t^a for all body areas a: second stage. How can we determine the remaining coefficients c_t^a?

Let us consider one of such yet-undetermined coefficients c_t^a. This coefficient describes the reaction of a body area a to the activation of an activation point t. As we have mentioned in our description of the first stage, for the body area a, there exists an activation point t' which is "most related" to this area. For this point, we know the corresponding coefficient $c_{t'}^a$ – it is equal to $1/x$, where x is the smallest activation of the point t' which causes a feeling in the body area a.

To determine the value c_t^a, we apply activation to *two* points t' and t: namely, we apply, to t', an activation $x - \varepsilon$ which is slightly smaller than x (and therefore, by itself, does not cause any feeling in a), and then start and slowly increase the activation of t until the patient gets a feeling.

If $c_t^a \neq 0$, then, for sufficiently small ε, this can be achieved by an arbitrarily small activation $x(t)$. The resulting activation is close to the activation x which is known not to cause any danger, so it will also not cause any danger in any body area.

The actual value of the coefficient c_t^a can be determined from the condition $c_{t'}^a \cdot (x-\varepsilon) + c_t^a \cdot x(t) = 1$, where $x(t)$ is the smallest value of the activation of t at which a patient starts feeling something in the body area a in this 2-point activation. We know $c_{t'}^a$, x, ε, and $x(t)$, and therefore, from this condition, we can determine the desired coefficient c_t^a as

$$c_t^a = \frac{1 - c_{t'}^a \cdot (x - \varepsilon)}{x(t)}.$$

7.3 The Optimization Problem

When we know all the coefficients c_t^a, then the question of what activations to apply becomes a precise mathematical problem: to find the values $x(t)$ for which:

- there is no discomfort in any body area, i.e., $\sum\limits_t c_t^a \cdot x(t) \le y_a$ for all a;
- there is an effect in all body areas affected by chronic pain, i.e., $\sum\limits_t c_t^a \cdot x(t) \ge 1$ for all such a; and
- there is no effect in body areas in which there is no pain, i.e., $\sum\limits_t c_t^a \cdot x(t) < 1$ for all such a.

This is a linear programming problem, and it can be solved by known algorithms for solving such problems.

If it is not possible to find the ideal solution, then we can, e.g., search for a solution which, instead of not affecting unnecessary body areas at all, minimizes the total effect in these body areas, i.e., minimizes the value

$$\sum_a \min\left(\sum_t c_t^a \cdot x(t) - 1, 0\right),$$

where the sum is over all ideally-unaffected areas a. This optimization problem can also be solved by linear programming techniques.

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