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A rule-based expert system for real-time feedback-control in deep brain stimulation

Abstract: Programming in deep brain stimulation (DBS) is often a labour-intensive process. Although automatic closed-loop stimulation has recently been receiving considerable attention, it is still far from clinical settings. Testing in-loop stimulation in a clinical setting is extremely challenging due to manual programming and the lack of synchronisation between stimulation and monitoring devices. In this work, we present a simple rule-based expert system to test feedback-controlled DBS in a clinical setting. The new application operates in closed-loop with the physician as acting person and real-time feedback from an accelerometer. Patients with movement disorders such as in essential tremor announce an individually acceptable level of tremor as a boundary condition for control. As a proof-of-concept, the expert system provides continuous recommendations of stimulation parameters and guides the physician to increase or decrease DBS amplitude by capturing tremor acceleration power on the patients' forearms. The introduced application considers the technical and practical aspects in a clinical setting. Data obtained from test subjects provide insight into tremor dynamics. We demonstrate the clinical applicability of the rule-based control system for future research focusing on tremor dynamics and in-loop stimulation. Finally, a telemetry streaming system could provide the interface for the application of automatic tremor control without the physician as acting person.

Keywords: Movement disorders, essential tremor, wearable motion sensors, rule-based expert systems, deep brain stimulation.

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1 Introduction

DBS is an established method for the treatment of movement disorders such as in Parkinson's disease (PD) and essential tremor (ET). The device-based therapy, however, is associated with a time-consuming programming including frequent patients' visits, involvement of movement disorder experts and sometimes non-optimal therapeutic effects [1]. These time- and resource consuming procedures further increase the socio-economic burden [2]. The next frontier in personalised medicine, is to deliver feedback therapy and to go beyond the open-loop DBS. So far, the literature has reported a large amount of theoretical and simulation works related to closed-loop DBS for movement disorders, which are, however, typically far from a real-world clinical setting [3]. An exception is a commercially available and approved closed-loop neuro-stimulation system for cortical stimulation in epilepsy [4].

In clinical practice, the physical examination of motor symptoms includes a series of standardised movement tasks. In parallel, the physician adapts the DBS parameters to suppress the motor symptoms by visual inspection of the movement tasks [5]. An accurate estimation of the motor symptoms, such as tremor in PD is strongly dependent on the observational skills of the clinician [5], [6]. More objective and precise methods that contribute to the evaluation of motor symptoms and the programming of the DBS parameters may support the clinician [6]. Inertial sensors such as accelerometers provide reliable feedback to quantify tremor, which in turn may help to adapt DBS parameters [1], [7].

A rule-based expert system, for example based on fuzzy logic, combines human heuristics with computer-aided decision making. The natural heuristic rules are modelled as linguistic expressions that reflect the human experience [8]. Several practical application of fuzzy logic control on industrial processes have been reported [9]. Moreover, fuzzy logic is highly applicable for the development of knowledge-based systems in medicine, such as disease diagnosis and optimal treatment selection. An example is a fuzzy inference system used to identify tremor episodes [10].

In this work, a simple rule-based expert system for a feedback-controlled parameter tuning in DBS is developed. The main objective is to demonstrate the clinical applicability of the rule-based control system for future research focusing on tremor dynamics and in-loop stimulation. Ultimately this will minimise tremor while reducing the total electrical energy delivered (TEED) [11] to the brain compared to the initial standard DBS parameters, which are typically set high.

2 Methods

This work mainly describes the design of the feedback loop and a simple rule-based expert system. The system is designed with a custom written MATLAB™ software (R2018a, MathWorks Inc., USA). Sensor data is transmitted to this software via Bluetooth™ from a *Shimmer3 IMU* sensor (Shimmer™ Corp., Ireland) [12]. Tremor data is sampled at a frequency of 200 Hz. Based on 20 test measurements, the total execution time for processing, analysis and visualisation of the data streams in the MATLAB™-based software was estimated to be less than 200 ms. In addition, a graphical user interface (GUI) was developed, which guides the physician to increase or decrease the DBS amplitude. The 3-axis acceleration data of the inertial measurement unit (IMU in *Shimmer3*) are filtered in real-time by a 2-pole digital Chebyshev filter [13] around the tremor dominant frequency. Subsequently the acceleration norm signal is calculated.

2.1 Tremor power curve

To capture tremor dynamics, the magnitude squared of the short-time Fourier transform (STFT) [13] is computed from the acceleration norm signal. This feature is defined as a tremor power curve and implemented in the rule-based expert system for tremor control in real-time. Short time windows are defined with an overlap of one data sample by default. The window length depends on the DBS response time to supress the tremor of the individual patient. It may differ for each DBS parameter change. Hence, an average value is estimated for each patient by the visual inspection to the response times. The STFT was modified by Hann windowing to reduce the spectral leakage [14]. Tremor power is estimated from the area under the curve of each STFT window and the data values are consecutively arranged. Note that the execution time of the tremor power curve is dependent on the window length as well as on the displayed time span of the free-running signal in the GUI. Real-time buffers process the streamed data packages for filtering and visualisation.

2.2 Study cohort

In this case study, ET patients were selected after a careful screening process. The study was conducted at the Centre Hospitalier de Luxembourg (see Author Statement). Inclusion and exclusion criteria were defined on the basis of the guidelines at the hospital. The patients followed the daily medication intake including primidone and propranolol.

2.3 Control system design

The design of the feedback control loop is based on the objective understanding of the tremor dynamics analysed in previous experiments. Figure 1 represents the control system configuration, where the major elements are identified as the rule-based expert system, physician with the DBS programmer device, the accelerometer, and the tremor patient.

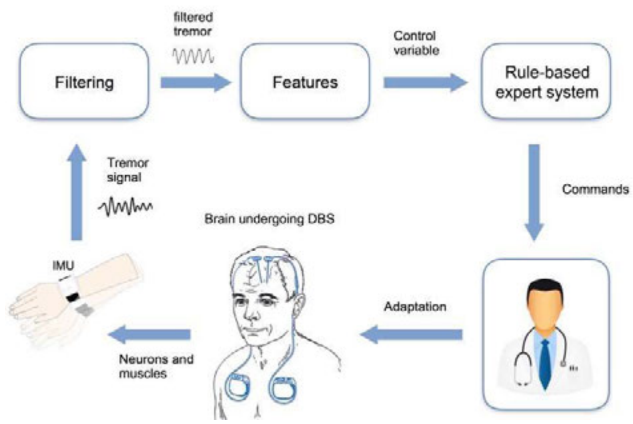

Figure 1: A simple rule-based system for real-time feedback-control in DBS. To describe the dynamics of the controller, the control surface is obtained from approximations based on a collection of IF-THEN rules as logical implication.

Patients announce their acceptable level of tremor as a boundary condition for control. A deadband is defined around the acceptable level of tremor in which no action occurs by the expert system in order to prevent high-frequency toggling of the DBS parameter commands. The operational space for control is spanned by low-power and high-power bands to drive the tremor power curve back into the deadband in the presence of unwanted disturbances. Power bands were defined for each patient individually. From this operational space, we investigated how to impose constraints on the different boundaries of the power bands, in order to obtain a strategy of boundary findings. Upper and lower limits of the deadband, low-power, and high-power bands are defined based on experimental tests. The definition of the bounds depends on the tremor severity and the response time of the patients to the DBS. Both define the key control parameters of the rule-based expert system. The performance of the system is evaluated after each examination based on the analysed accelerometer data. Moreover, a one-sample-ahead forecasting (i.e. exponential smoothing technique) is applied to the tremor power curve to reduce strong tremor fluctuations around the deadband [16].

2.4 Rule-based expert system

The efficiency of DBS programming depends strongly on the observation, intuition and knowledge of the clinician. The proposed control strategy in this work mainly uses the insights gained from previous examinations and forms it into a number of IF-THEN rules as logical implication for the rule-based expert system. For the proposed method, a total number of 5 linguistic variables were defined for 5 inputs with rectangle membership functions. The rule-based controller operates in different power bands when the actual tremor power curve is outside the deadband as described in Table 1. In this case, the physician will change the DBS parameters with the clinician programmer device based on the instructions of the rule-based expert system. As an example, tremor power bands were defined according to the rate of change of the DBS amplitude in a clinician programmer device (Table 1). The stimulation parameter rate changes immediately when crossing a tremor power band and is updated after a fixed response time within a power band (see Table 1).

Tremor power (Process variable)	**Tremor severity** (Heuristic classification)	**Rule-based decision** (Linguistic expression)	**Stimulation rate** (Control variable)
Power > X4	high tremor	high increase, wait response time, repeat	up 0.5 V if amplitude < max*
X3 < Power ≤ X4	tremor increase	low increase, wait response time, repeat	up 0.1 V if amplitude < max*
X2 < Power ≤ X3	acceptable tremor without side effects	no change of stimulation	+/- 0V
X1 < Power ≤ X2	slight tremor	low decrease, wait response time, repeat	down 0.1 V if amplitude > 0 V
Power ≤ X1	absent tremor	high decrease, wait response time, repeat	down 0.5 V if amplitude > 0 V

Table 1: Operational modes of the rule-based expert system. Tremor power bands were defined for each patient individually by experimental testing with lower and upper bounds (variable X) for the deadband (grey shaded area), low-power bands (below grey shaded area) for low and high DBS decrease, and high-power bands (above grey shaded area) for low and high DBS increase. Stimulation parameter changes in each power band (deadband excluded) were updated (*repeat*) after a fixed response time. Switching between stimulation rates, i.e. low decrease/increase or high decrease/increase, are displayed immediately. *Stimulation parameters are updated until the stimulation limit is reached. This was determined by stimulation induced side effects such as headache, tingling or cramps in the arms. However, this may not prevent supra-therapeutic effects from occurring when high stimulation is applied close to this upper limit [17]. Note that the safety of the patient is the ultimate objective and hence requires a visual check before each DBS parameter increase.

3 Results

The rule-based controller was tested in clinical settings as well as on a vibration exciter for the technical validation. Our method is particularly well suited for ET patients who show a nearly linear response to DBS. A previous study confirmed this observation in a moderate number of ET patients [18]. As an example, the result of an ET patient with isolated tremor syndrome is shown in Figure 2 (excerpt). This type of tremor is typically not associated with a rest tremor, i.e. mixed-type tremor syndrome. Note that hand tremor in rest position is likely to occur in up to 20% of the ET patients [19].

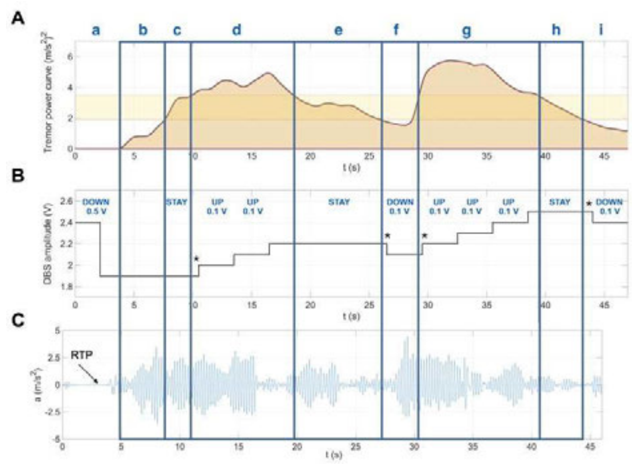

Figure 2: An example of controlled programming in DBS using the expert system. Tremor time series data of an ET patient with right hand postural tremor. (**A**) Deadband (yellow shaded area) and the smoothed tremor power curve (brown signal, with total power as shaded area) were computed as a feature based on the STFT. (**B**) Stimulation amplitude changes (black step function) with the control commands of the expert system (blue) are shown. The clinician followed the rule-based instructions immediately. Initial parameters were: 2.4 V, 130 Hz, and 60 µs (Medtronic^{TM}, lead 3389, C2- with 1223 Ω) with a TEED of 36.36 µJ. Note that the setpoint was at around 2.3 V. Side effects (muscle cramps) occurred at around 3.1 V. DBS parameters were adapted with the clinician programmer device. (**C**) For illustration purposes, the first principle component score of the band-pass filtered acceleration signal (blue) is presented instead of the acceleration norm signal. Note that the delay (negative signal shift) is mainly caused by the STFT. Trembling occurs after the transition from rest-to-posture (RTP, black arrow).

In Figure 2, each accelerometer signal axis was band-pass filtered ±2 Hz around the tremor-dominant peak frequency of 4.4 Hz and the norm signal was computed. The tremor response time was estimated to be less than 2 s. To compute the smoothed tremor power curve, a STFT with a 1.5 s window was selected. The operational mode of the expert system is pertaining to low-power bands (i.e. low decrease or increase of the stimulation rate) only (see Table 1). Note that the upper bound of the low-power band (i.e. low increase of the stimulation rate) was obtained when side effects occurred. The lower bound for the low-power band is zero amplitude. DBS amplitudes were updated every 2 s within the low-power bands in Figure 2 (see B, area d and g). Switching between the stimulation rates, e.g. from the deadband to the low-power band are displayed immediately in Figure 2 (see A and B; i.e. boundary between c and d, e and f, f and g, and h and i). Note that mainly through the computation of the STFT and the displayed time span of the free-running signals, a total delay time of about 2 s occurred (see asterisk in B). In the final step, the physician followed the commands of the rule-based controller (see **B**, commands in blue).

4 Discussion

This work demonstrates the clinical applicability of the rule-based control system and provides a platform for further research work. Note that the implementation of a fuzzy controller without a telemetry streaming system remains challenging in a clinical setting. As an example, Nexus-D (Medtronic^{TM} plc., Ireland [7]) could provide the interface to implement fuzzy membership functions and apply automatic tremor control in the clinical setting without the physician as acting person.

The definition of power bands (high, low, deadband) and the rate of change of the DBS parameters depend on the clinical testing, human delay time of the clinician, and settings of the DBS programmer device. These parameters describe the sensitivity of the rule-based feedback control system. Strong tremor dynamics such as in Parkinson's disease patients [20] may limits the number of examinations and needs further investigation. Moreover, the acceleration power bands are static and this requires a frequent update of all the parameters. Patients with linear tremor behaviour are preferred to test the introduced control approach. Finding the suitable parameters, however, is a compromise between tracking speed and symptom suppression.

5 Conclusion

This work presents a simple rule-based expert system for testing closed-loop DBS in ET patients. The novel clinical application provides a platform for future research work focused on tremor dynamics and closed loop DBS. Clinical research devices with a telemetry streaming system could provide the interface to apply automatic tremor control with imprecise membership functions.

Author Statement

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