

Decision Support Systems: Improving Levels of Care and Lowering Costs in Anticoagulation Therapy

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Abstract. The objectives of this work in progress are to improve the levels of care in anticoagulation therapy while reducing the effort required and the costs. This will be achieved by the preprocessing of the available real world data and projecting it into a suitable analysis space before modelling with individualised, constantly learning Evolving Takagi Sugeno [1] and Connectivist Network-type models whose structure and parameters are the result of extensive research. It is hoped that this will lead to accurate predictions of the future levels of anticoagulation from a given dose recommendation.

Keywords: Decision Support Systems, Classification, Prediction, Anticoagulation.

1 Introduction

The increasing age of the population is a significant factor in the increasing demand for anticoagulation therapy [2]. The preferred treatment is an orally administered Vitamin K antagonist, typically Warfarin. Such treatment is both risky and expensive. Under-anticoagulation increases the risk of a thromboembolic event and over-anticoagulation increases the risk of haemorrhage. The coagulability of the blood is measured in International Normalised Ratio (INR) units. The medical goal is to keep this value within an indication-specific therapeutic range. Clinicians are only able to achieve this for 50% of the duration of treatment [3]. There is clearly room for improvement in the level of care. Regular clinic visits are costly and do not lead to a good patient experience.

Decision support systems have been widely used in anticoagulation clinics since it was shown that they perform at least as well as the clinicians [4]. Often the software includes workflow functionality specific to anticoagulation clinics and uses a proprietary algorithm to recommend a dose and test interval. Even with such software clinics rarely achieve better than 70% of a patient's time in the therapeutic range [5]. The challenge here is to increase the time patients spend inside their therapeutic INR range. This will reduce the number of clinic visits with the associated benefits of reducing costs and improving the patient experience and quality of treatment. This retrospective study uses anonymous anticoagulation data collected in the DAWN AC Decision Support Software for a benchmarking service which aims to improve care at participating clinics. Data is available from five unknown clinics for five six month

periods from April 2003 to October 2005. Data is available for 19585 patients and represents around 50000 patient treatment years. This huge volume of real world anticoagulation data offers an excellent opportunity to study patients' INR time series in detail and should ensure that the results can be generalised to the wider community of patients.

2 Methods and Challenges

The goal is to enhance the results achieved by the DAWN AC System using new INR time series modelling techniques that complement the existing algorithm. This will allow for the accurate prediction of a patient's future level of anticoagulation based on a current Warfarin dose and next visit interval recommendation. Thus the aim here is to help the clinician to arrive at a better dosing decision with less effort and therefore obtain more stable INR levels and longer test intervals. It is known that patients react quite differently to the same dose of Warfarin and that their responses change over time. Hence two key ideas are proposed:

- modelling of INR responses on a per individual basis, over and above common behaviours
- update of patients' models at every clinic visit to learn previously unseen responses

These two simple ideas should bring an improvement in modelling. Other key enablers are:

- sensible pre-processing of the extensive real world anticoagulation data, in order to remove unrealistic outlying values
- novel representations of the data in the input space
- the use of powerful modelling techniques, namely Evolving Takagi Sugeno (eTS), eClass [6] and network-type models respectively
- new visualisation methods will help the clinician identify unusual and/or dangerous patterns in the INR time series

The key challenge in assessing the impact of any given Warfarin dose recommendation is the number of other factors that affect the coagulability of the blood. Many of these factors are not measured or reported to the clinician during the visit. Typical factors are dose compliance, drug interactions (Aspirin, Paracetamol, Amiodarone, Antibiotics, and more), lifestyle (smoking, drinking, and exercise), diet, general health, and the time elapsed between the latest dose and the clinic visit measurement of the INR. Furthermore, there is noise in the measurement and recording of INR values. Due to the above reasons, it is immediately apparent why excellent levels of care (treatment quality) are very difficult to achieve.

3 Experimental Results

Currently two types of INR modelling techniques have been developed and tested using real data: a real-valued point prediction of the next INR measurement [7] and a classification prediction if the next INR reading will be in or out of the therapeutic

range. The simpler INR classification method has proved to be very effective. A single real value between zero and one is produced by the network model while the eClass model (a classifier built on eTS technology) produces two real numbers which are normalised before the optimum decision boundary is selected based on the classic Receiver Operating Characteristic Accuracy measurement. This is calculated by dividing the total number of TRUE predictions by the total number of predictions. Furthermore, the True Positive Rate (TPR) and True Negative Rate (TNR) give an indication of how well each class is predicted. After preprocessing the entire data set 14181 patients remained of which 1000 were used to train the models before testing the proposed schemes with the remaining 13181 patients (comprising 404023 clinic visits). The peak accuracy results are presented in the table in figure 1 below. It is interesting to note that eClass performs well even though it is not being used optimally. eClass and eTS are designed for online operation starting with no pre-training, whereas here the eClass model is pretrained for equivalence with the network. The models' average time taken to estimate the next INR measurement and then adapt to the measured value can also be found in the in figure 1. eClass operates much more quickly than the network-type model. Further to this, eClass and eTS maintain a rule base of the form:

if (INR is x) and (dose is y) and (interval is z) then (next INR is a)

This can provide some understanding of the INR response to dosing instructions for the clinicians. Networks are 'black box' models where the internal weights and bias values are not interpretable at the application level.

Table 1. Table of Classification Accuracy of the Dawn AC, eClass (eTS), and Network-type Models

System	Max Acc (%)	TPR (%)	TNR (%)	Average Time per prediction and train (seconds)
Dawn AC	56.8	56.8	0	N/A
eClass	74.4	65	52.7	0.0046
Network	89.1	83	88.6	0.328

Real values of the next INR reading are more difficult to predict. Using the fuzzy rule-based eTS method with preprocessed data and transformation of the input data a mean squared INR prediction error (MSE) of 0.375 has been achieved for 1000 train patients and 1000 test patients. Using exactly the same data, a network-type system produces an average INR prediction MSE of 0.987. Both types of model adapt with a patient's changing responses but eTS has the advantage of achieving this by changing its internal structure whereas networks change their internal weights but not their structure.

4 Conclusions and Future Work

These results show that a more sophisticated modelling of patients' INR responses is possible if the input data is carefully preprocessed and projected into a suitable input

space. These transformations separate the influence of the different factors (as discussed above) from the actual Dose/INR response mechanism allowing both to be modelled separately. The two category classification of whether the following INR measurement will be in or out of range is very accurate. The connectivist network-type models outperform eClass in terms of classification accuracy but they do not provide any understanding of the problem and work two orders of magnitude slower. A three way classifier will be developed. A final step will involve suggesting optimum dosing recommendations (both Warfarin dose and visit interval). Work is under way to improve the existing real-valued INR prediction results.

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