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Graphical analysis of the progression of atrial arrhythmia through an ensemble of Generative Adversarial Network Discriminators

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Abstract

Logs of arrhythmia episodes in patients with pacemakers are used to estimate the temporal progression of atrial arrhythmia. In order to attain an early detection, a stream of dates and episode lengths are fed to an array of detectors, each of which is responsive to a narrow range of arrhythmias. The outputs of these detectors are organized on a projection map, used by the specialist to assess the risk in the evolution of the patient. Each of the mentioned detectors is a Recurrent Neural Network(RNN), that is in turn the discriminating element of a Generative Adversarial Network (GAN) that has been trained to generate temporal sequences of values of the degrees of truth that the arrhythmia episodes are not isolated.

Keywords: Heart Disease, Generative Adversarial Network, Time Series

1 Introduction

Atrial fibrillation (AF) is an abnormal heartbeat, common in the elderly, that sometimes progresses from paroxysmal arrhythmia (episodes of arrhythmia that end spontaneously) to persistent arrhythmia (episodes that last more than seven days and do not end without external intervention) or permanent arrhythmia (uninterrupted episodes). It is common for paroxysmal arrhythmia to progress to persistent or permanent arrhythmia [7]. There are numerous risk factors that influence the progress [8], and early diagnosis is beneficial for optimal treatment.

The treatment of AF often involves the use of pacemakers or ICDs (Implantable Cardiac Defibrillators). These devices keep a record of the dates and lengths of the episodes, and (to a certain extent) intracardiac electrograms (iECGs) of these. Although surface electrograms are a potential source of information about the evolution of the arrhythmia [6], the morphology of the heartbeat in iECGs is lost in the high-pass filtering at the ICD electrode and the only relevant information is kept in the instantaneous frequencies of atrium and ventricle (see Figure 1). On the other hand, an early diagnosis is needed, thus the working records are necessarily short (see Figure 2), and it may well happen that the number of available episodes for a given patient is not large enough to fit a non-trivial model. This is aggravated by the fact that the data is non-stationary and it is precisely the change in the properties of this data (from paroxysmal to permanent) that we want to predict on the basis of a short sample of data. Additional complications exist, because the algorithm that the pacemaker uses for determining episode lengths is not reliable and clusters of short episodes are wrongly reported sometimes instead of long AF episodes. All in all, sequences of episode lengths cannot be used isolatedly; a model that jointly depends on both the lenghts and the time lapses between episodes is needed.

Unfortunately, although the progression of AF is a complex process that depends on many different factors, each patient is associated to only a few tens of pacemaker records. There are not many different techniques for classifying short time series [5] and, to the best of our knowledge, a model that is simple enough to be learnt from a small set of data while at the same time it is able to extrapolate the break point between paroxistic and permanent AF has not been found yet.

Unlike this kind of model, this paper follows a different approach. A set of dynamical models that are able to capture the key features of the different AF progressions will be used, but these models will not be fitted to the data, but used to enlarge the training sample. An array of learning detectors of AF are trained with model-generated data, so that each of the detectors is only exposed to arrhythmias of a certain type. When

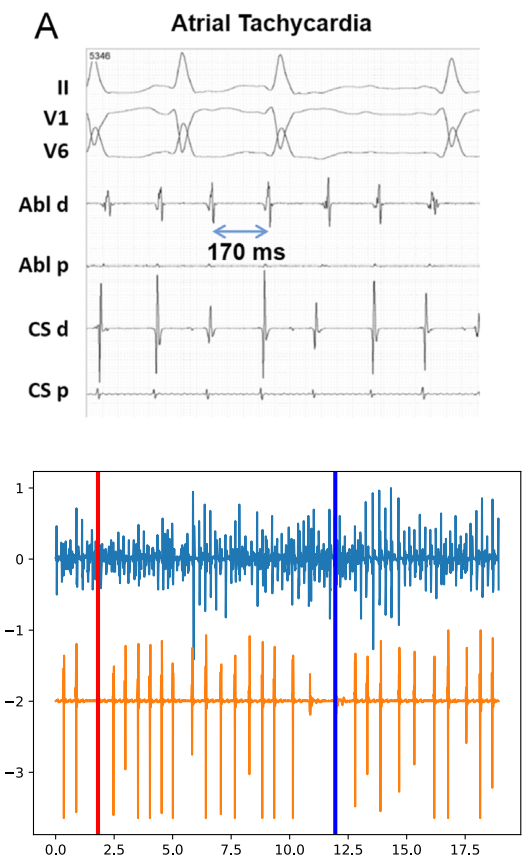

Figure 1: Top: Surface ECG (taken from reference [1]). Bottom: Intracardiac ECG. The morphology of the surface ECG is not kept in the iECG, where there is only one peak for each heartbeat.

this array is fed with pacemaker records from a real patient, it is expected that only a few detectors will recognize that the patient's arrhythmia is the same type as the arrhythmia with which they were trained.

Key to the success of this idea is the specificity of the detectors, that must only react to episodes matching a compact set of clinical situations. In this paper it was considered that detectors obtained from Generative Adversarial Networks (GANs) can be highly specific. In particular, two recurrent neural networks will be used as generator and discriminator, and trained until the generator is able to produce realistic sequences of arrhythmia episodes and the discriminator efficiently separates these sequences from "actual" sequences (in this case, "actual" series are synthesized with the dynamical models mentioned before).

In any case, when these detectors are fed with insufficient data (short pacemaker records) it is expected that many of them recognize the arrhythmia as its own, thus the output of the set of detectors will not be too specific. It is also proposed that these detectors are organized in a map [4]. If detectors tuned to arrhythmias with similar properties are adjacent in the map, the output of the map can be regarded as a projection of the available data on the parameter space of the dynamical models. This projection provides a depiction of the parameters of the model that best fit the patient and also gives insight about the narrowness of the estimation that is possible with the available data.

The structure of this paper is as follows: in Section 2, pacemakers and the dynamical model of the AF episodes are described. In Section 3, the GAN used as a detector is introduced and the map arrangement described. In Section 4 some preliminary results about the specificity of the detectors and the application of this technique to actual patients are given. The paper concludes in Section 5 with a discussion about the potential advantages and drawbacks of this idea and the areas of further development.

2 A model of pacemaker-detected arrhythmia events

A surface electrogram (ECG) is the representation of cardiac electrical activity from two electrodes placed on the surface of the body which are located apart from the heart (see Figure 1, upper part). With this type of derivation, all kinds of electrical activity are recorded, including non-cardiac electrical activity. On the contrary, an intracardiac electrocardiogram (iECG) (recall Figure 1, lower part) is the representation of the potential difference between two points in contact with the myocardium in space over time. iECGs are obtained from pacemakers or ICDs logs and are less informative. The purpose of this study is to anticipate arrhythmia progress on the basis of these pacemakers or ICDs logs.

Pacemakers do not store a continuous stream of data, but there are certain events that trigger that data is recorded. The primary purpose of a pacemaker is to release an electrical current between two points to activate the cardiac cells and therefore facilitate cardiac contraction. Depending on the electrical signal that is measured through the leads, the pacemaker will respond in order to stimulate, inhibit, or change its operation mode. In particular, in the presence of cardiac arrhythmia, if a patient experiences a high intrinsic atrial heart rate the pacemaker does not try to match the ventricle to the atrial rate. Instead, the pacemaker changes its operation mode and uses a different algorithm for generating the excitation of the ventricle. This process is called Automatic Mode Switching (AMS) [3]. AMS events are stored in the pacemaker memory and are used to mark the beginning of AF episodes (recall Figure 2, upper part). The lengths of

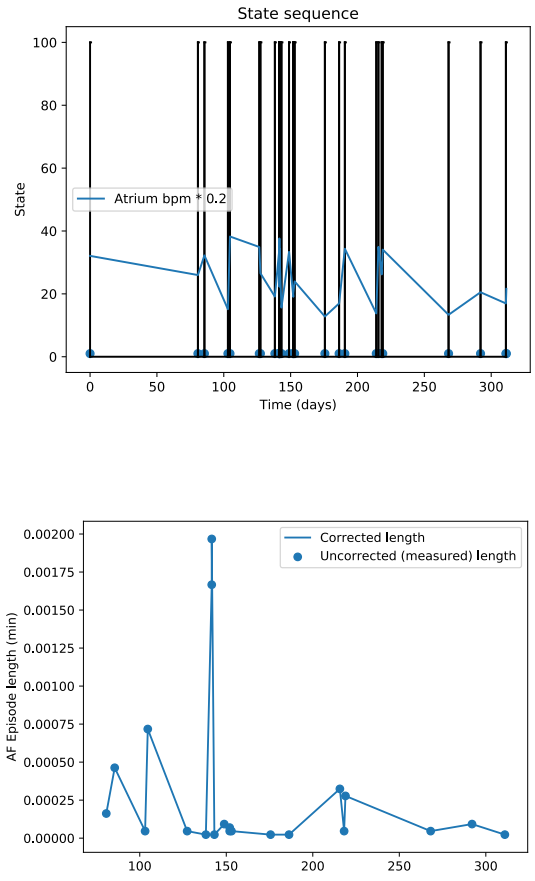

Figure 2: Top: Dates of pacemaker mode changes during a year (beginning of AF episodes, see also Figure 1). Bottom: Recorded length of the AF episodes.

the AF episodes are stored along with the AMS dates in the pacemaker memory.

Although AMS is a simple concept, the mode switching depends on a large number of variables that depend on the patient. It is possible that the peacemaker algorithm prematurely concludes that the AF event has ended, only to discover past a few seconds that an AF is still taking place. In this case, a second AMS event is generated and the pacemaker mode is restored. This has not relevant consequences for the efficiency of the device, but the stored information is inaccurate, as there may be cases where a cluster of short arrhythmias is reported instead of a long event.

2.1 Dynamical model of AMS events

A simplified model of the temporal sequence of AMS events associated to a patient is depicted in Figure 3. This is a continuous time Markov model with three states: (1) normal/out of arrhythmia, (2) arrhythmia and (3) gap. The third state is associated to those cases where the pacemaker has detected a non-existent ending of the event and a new AMS event is going to happen. Observe that there are AMS events in the transitions from normal to arrhythmia but also in transitions from gap to arrhythmia.

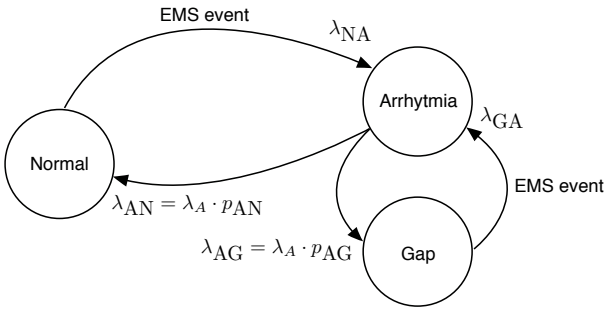

Figure 3: State diagram of the dynamical model of the beginning of AF episodes.

The times at states "normal" and "gap" follow exponential distributions with parameters λ_{NA} and λ_{GA}, respectively. The time at the state "arrhythmia" follows an exponential distribution with parameter λ_A. The probability that the next state after "arrhythmia" is "gap" is p_{AG} and the probability that this transition ends in "normal" is $p_{AN} = 1 - p_{AG}$.

The progression of the AF from paroxysmal to permanent is introduced by letting the parameter λ_{NA} change with time. The speed of the progression is modelled by a parameter $\alpha \in [0, 1]$,

$$\lambda_{NA}(t) = \lambda_{NA}(0) \cdot \alpha^t, \tag{1}$$

where $\alpha = 1$ is an stable patient and lower values of α are patients with a quick progression to permanent arrhythmia.

3 GAN-based detector

The simple Markov model described in the preceding section captures the essence of the pacemaker operation: it takes into account the frequency of the AF events, its length, the inaccuracies of the pacemaker and the speed of the progression. However, there are patients that do not fit this model, because the time between AF episodes does not always follow an exponential distribution. Also, as mentioned in the introduction, a large set of AF episodes is not compatible with an early diagnosis thus the numerical estimation of the five parameters λ_{NA}, λ_{GA}, λ_A, p_{AG} and α would not be reliable even in the case that the patient fits the model.

The procedure that is proposed in this study relies

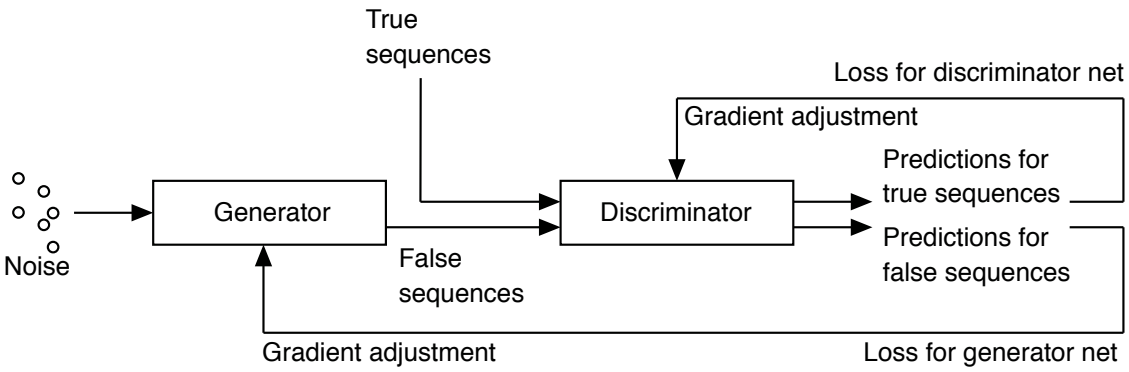

Figure 4: GAN architecture for obtaining one of the discriminant elements

in an array of discriminant elements, tuned to specific sets of values of the five parameters that define an instance of the Markov model. The output of these elements is a projection of the episode in a five-dimensional space whose coordinates are the values of λ_{NA}, λ_{GA}, λ_{A}, p_{AG} and α. λ_{GA} and p_{AG} depend on the pacemaker algorithm, while λ_{NA}, λ_{A} and α measure the condition of the patient. In particular, α measures the progression of the AF. Each of these elements is trained with different sequences of AF episodes generated by means of a model that depends on a given tuple of values of the parameters. If these discriminant elements are specific enough (i.e. if they only react to sequences of values that are generated with the same or similar parameters as the training sequences) it is immediate that, when confronted to a time series that follows the model in Section 2.1, only one element of the map will be active. When a sequence of AF episodes of a patient whose progression do not exactly matches the model is fed to the map, a pattern of activations will be displayed that allows to assess the progression speed of the arrhythmia.

In order to obtain the discriminant elements, a GAN is used with the architecture described in Figure 4. Both the generator and the discriminator are LSTM networks. The output of the discriminator is a voting combination of all the nodes in the LSTM network, that is compared to a threshold in order to decide whether the input is one of the true sequences or it is the output of the generator LSTM. The input to the net is a sequence of fuzzy memberships of the assert "the AMS event is isolated", which measures how many events are present in a soft window (with Gaussian membership) that spans a few days before and after the data and moves along with the data (see Figure 5) [9].

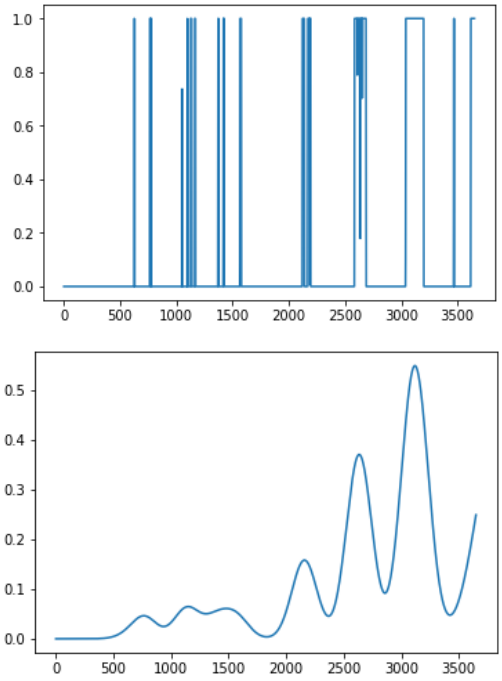

Figure 5: Top: Synthetic sequence of episodes (simulation time: 10 years), showing the evolution to permanent AF. Bottom: Sequence comprising the degrees of truth that AF events are isolated (input to the GAN network)

4 Numerical results

Properties of the GAN discriminators are analyzed first in terms of the sensibility of the nets to changes in the parameters, namely the ability of an LSTM network for correctly classifying Markov model-produced sequences in terms of the generating model parameters. At the end of this section two maps are shown, measuring both a synthetic sequence of AMS events and a true patient.

The experimental setup is as follows: the code for training GAN recurrent networks for time series has been adapted from the publicly available code at `https://github.com/ratschlab/RGAN` [2]. The input to the net has a batch size of 28, sequence length of 73 and one feature. The loss function of the discriminator net is the fraction of misclassifications. A total of 14000 sequences have been generated for each combination of parameters chosen for the Markov model.

4.1 Sensibility of the LSTM detector

A brief study about the sensibility of the LSTM detector has been included in Tables 1 and 2. The first table collects the results for $\alpha = 0.998$ (fast progression), and the second table contains the same experiments for $\alpha = 0.999$ (slow progression).

The meaning of the rows and columns of these tables is as follows: each column contains the fraction of correct classifications of a discriminator that has been trained with sequences produced by the Markov model seen before. The values of $\lambda_{\mathrm{NA}}(0)$ used for computing these sequences are indicated in the column labels. The first and second rows, "Train" and "Test" are the percentage of correct detections of "True" sequences (Markov models) vs. "False" sequences (produced by the generator net). The rows labelled $\alpha = 0.997 \ldots 0.999$ are the fraction of sequences with the same parameters as those used for training the net but a different parameter α. The remaining rows are the fraction of correct classifications when the net is fed with sequences with a different value of λ_{NA}.

These results show that the detectors are highly responsive when the arrhythmia is paroxysmal (low values of λ_{NA}, thus time between episodes is high). This is the desired result, because these are the cases with clinical interest. The net is less capable when λ_{NA} is high, however these are the cases where the patient is in a permanent arrhythmia condition at the beginning of the experiments thus the evolution of the patient is self-evident.

4.2 Projection map

Two maps (see Figure 6) were selected for illustrating the method. The horizontal axis is labelled β, which is the inverse of the parameter λ_{NA}, and can be understood as the expected number of days between two AF episodes at time $t = 0$. The vertical axis is labelled α and measures the speed of the progression. The lower the value of α, the quickest the progression to permanent AF.

The first map (Figure 6, left) depicts the output of an array of discriminators when the input is a synthetic sequence of AMS events, generated by means of the Markov model, with $\lambda_{\mathrm{NA}} = 1/90$ and $\alpha = 0.999$. It is expected that only one of the detectors reacts to this artificial sequence, and this is in fact the result (dark red area at $\beta = 90$ and $\alpha = 0.999$)

In the right part of the same Figure there is a second map with a projection of a sequence of AMS events taken from an actual pacemaker (see also Figure 7, where these episodes are shown). The dates of these AMS events are shown in the lower part of the same figure. The sequence of events does not follow the Markov model anymore, thus a clear identification as that shown in the map to the left is nowhere to be found, but nonetheless the projection of the sequence in the parameter spaces gives us a clear insight about the evolution of the patient. In particular, the dark red area in the bottom part of the map is compatible with a value of $\lambda_{\mathrm{NA}} \approx 1/200$ and also with a fast progression to permanent AF, $\alpha = 0.998$. The red region is also compatible with arrhythmias in the range of $100 < \beta < 250$, i.e. slower evolutions from starting points with more frequent episodes cannot be discarded because the number of episodes is not too high, but the most probable diagnosis is that of quick progression to permanent AF.

5 Concluding remarks and future work

We have shown that iECGs from ICDs and pacemakers can be used to a certain extent for predicting the change from paroxysmal to permanent AF. The main difficulty is with the short length of the pacemaker records, that has been addressed here by means of a graphical projection of the sequence of AMS events in the parameter space of a continuous-time Markov model. If the data is enough for a clear diagnosis, the map produces an estimation of the patient condition and future evolution, and in those cases where the data is insufficient the map produces a set of estimations that can be subjectively assessed in order to determine whether the evolution is positive or not.

This is a work in progress and there are some unsolved difficulties. There are five variables, thus each patient produces a hyper-cube that has to be sliced and presented to the user in different graphics. A second projection that puts all the information in a 2D map would be preferred. On the other hand, the degrees of truth of the detectors are not easily equalized and a method different that the weighted vote of the LSTM elements should be studied. Lastly, the use of GANs has an intrinsic advantage, that is the obtention of the generator network. This second network has not been used yet in this study, but we intend to use it to extend the pacemaker records into the future and

	$\lambda_{NA} = 1.0/10$	$\lambda_{NA} = 1.0/30$	$\lambda_{NA} = 1.0/90$	$\lambda_{NA} = 1.0/180$	$\lambda_{NA} = 1.0/260$
train	0.9794	0.9804	0.9830	0.9868	0.9800
test	0.9779	0.97978	0.9811	0.9847	0.9797
$\alpha = 0.997$	0.5299	0.2523	0.5373	0.4324	0.4878
$\alpha = 0.999$	1.0000	1.0000	0.9979	0.3475	0.4424
$\lambda_{NA} = 1/5$	0.3333	1.0000	1.0000	1.0000	1.0000
$\lambda_{NA} = 1/10$	-	0.8162	1.0000	1.0000	1.0000
$\lambda_{NA} = 1/30$	0.9967	-	0.9505	0.9970	0.9983
$\lambda_{NA} = 1/90$	1.0000	0.9703	-	0.1369	0.1969
$\lambda_{NA} = 1/180$	1.0000	0.9994	0.0914	-	0.0312
$\lambda_{NA} = 1/260$	1.0000	1.0000	0.1494	0.0008	-

Table 1: Sensitivity of the discriminator for $\alpha = 0.998$.

	$\lambda_{NA} = 1.0/8$	$\lambda_{NA} = 1.0/30$	$\lambda_{NA} = 1.0/90$	$\lambda_{NA} = 1.0/145$	$\lambda_{NA} = 1.0/180$
train	0.9832	0.9823	0.9809	0.9825	0.9838
test	0.9821	0.9818	0.9818	0.9853	0.9783
$\alpha = 0.997$	0.9986	0.9987	0.9986	0.9986	0.9997
$\alpha = 0.998$	0.9998	0.9998	0.9956	0.9485	0.9809
$\lambda_{NA} = 1/5$	0.1543	1.0000	1.0000	1.0000	1.0000
$\lambda_{NA} = 1/8$	-	1.0000	1.0000	1.0000	1.0000
$\lambda_{NA} = 1/30$	1.0000	-	0.9988	0.9997	0.9996
$\lambda_{NA} = 1/90$	1.0000	0.9978	-	0.1703	0.2002
$\lambda_{NA} = 1/120$	0.9800	0.9800	0.0012	0.0516	0.0566
$\lambda_{NA} = 1/145$	1.0000	1.0000	0.0001	-	0.0357
$\lambda_{NA} = 1/260$	1.0000	1.0000	0.0000	0.0008	0.0089

Table 2: Sensitivity of the discriminator for $\alpha = 0.999$.

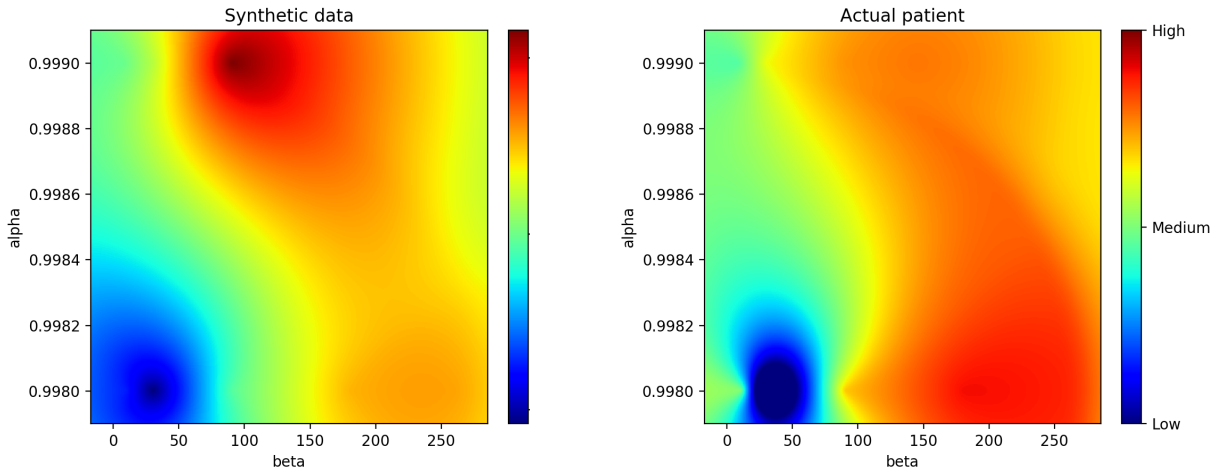

Figure 6: Left: projection of a sequence of AMS events generated by means of the Markov model, with $\lambda_{NA} = 1/90$ and $\alpha = 0.999$. Right: Projection of a sequence of AMS events from an actual pacemaker (see Figure 7). The map is compatible with a value of $\lambda_{NA} \approx 1/200$ and a fast progression to permanent AF, $\alpha = 0.998$

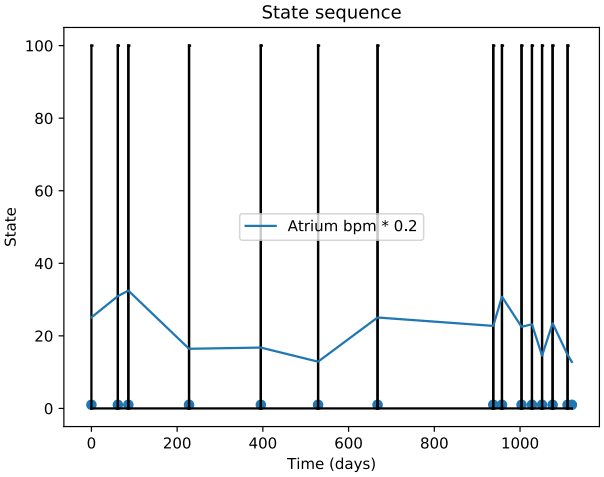

Figure 7: Dates of the AMS events for the patient in the right part of Figure 6

combine these extrapolated records with the estimation of α to improve the reliability of the estimation of the most important parameter, the speed of progress of the arrhythmia. In any case, a method is needed to prime the LSTM generator that can synchronize the state of this network with the sequence of measured records, and this method has yet to be developed.

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