# A unifying optimization approach of Mobitz- and Wenckebach-type cardiac blocks

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## Bachelorarbeit

vorgelegt von
Felix Bernhardt
geboren am 20. August 1992 in Haselünne,
Studiengang Mathematik.

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Betreut am Institut für Mathematische Optimierung von
Prof. Dr. rer. nat. habil. Sebastian Sager

# Contents

# List of Figures

# List of Tables

# 1 Introduction

Of all diagnosed medical conditions in Germany atrial flutter and atrial fibrillation are the fourth most common. In 2013 alone, 280,900 cases were recorded [1]. Atrial fibrillation is characterized by high-frequency chaotic electrical activation of the atria and an irregular ventricular response. Atrial flutter, on the other hand, is based on repeating circuits of electrical activation resulting in regular flutter waves [2].

Due to great differences in the treatment for both arrhythmias the right diagnosis is of paramount importance. Evaluating the regularity of the atrial activation would simplify an immediate diagnosis.

However, there exist only invasive methods which could reliably record the sinotrial conduction [3, p. 46]. Thus, detectection by easily measurable surface electrocardiogram (ECG) would be a great improvement both for patients and physicians.

Yet, distinguishing between both arrhythmias with the help of ECG measurements still poses great difficulties. This is because the distinct difference between atrial flutter and atrial fibrillation – the regular and the irregular atrial impulses respectively – does not at all times translate to distinct ECG patterns.

Due to the chaotic atrial activation the ECG measurements of a patient with atrial fibrillation show no predictable pattern. Despite regular flutter waves atrial flutter can also result in complex disturbances of the ECG. Therefore, it is very difficult to distinguish between the two phenomena by way of visual observation [2].

As for atrial flutter, this irregularity is caused by blocks within the atrioventricular (AV) node impeding the impulse conduction in the heart. They cover the actual regular atrial rhythm of atrial flutter. If this rhythm could be uncovered with the help of an algorithm, atrial flutter and atrial fibrillation could probably be correctly diagnosed using ECG measurements.

A first attempt was made by Scholz et al. using findings of the cardiologists Woldemar Mobitz and Karel Frederik Wenckebach. Mobitz and Wenckebach discovered that the ECG pattern caused by a disturbed conduction in the AV-node follows certain rules. They described two common phenomenological types of possible AV-blocks [4] [5] [3, p. 60].

Scholz et al. used these observations to develop an algorithm (MAVBA[1]) trying to reproduce certain characteristics of a measured ECG sequence. The quality of this simulation then indicates the proper diagnosis. This discrimination could be performed with a great accuracy so far [2]. However, the strict separation in Mobitz- and Wenckebach-type AV-blocks makes it difficult to also explain rare physiological phenomena. The objective of this thesis is to formulate and analyze the Q-model, a new approach which is not limited to two types of AV-blocks but rather can accommodate a more general class of AV-blocks. This new characterization may be able to further enhance the current diagnostic value of such decision support tools.

[1]Multi-level AV-block algorithm - labeling only valid within this thesis

# 2 Physiological Background

The anatomic and functional structure of the cardiac cycle is important to understand the idea behind MAVBA and the Q-model. Therefore, a small excursus to the physiological backgrounds is necessary.

## 2.1 Cardiac Cycle

The electrical conduction system dictates the cardiac cycle by creating and propagating impulses to the atria and the ventricles. The normal cardiac cycle, describing one complete beat of the heart, follows a specific routine. This routine is described in Table 1. The sinoatrial node, located in the right atrium, serves as a pacemaker. It provides the initial impulse. An emitted signal first stimulates both atria to contract while traveling to the atrioventricular node. After a short delay the impulse is transmitted through the His-bundle to the Purkinje fibers. These fibers are directly to the cells within the ventricle-walls. This causes the large heart chambers to contract. At the end of the cardiac cycle both chambers restore their resting state. This process is called ventricular repolarization [3, p. 61] [6].

The electrical conduction regulating this process results in the characteristic surface ECG intervals. In this thesis, the most important structure in these intervals is the easy recognizable R-complex. It indicates the contraction of the ventricles. Figure 1 shows the partition of one complete ECG interval.

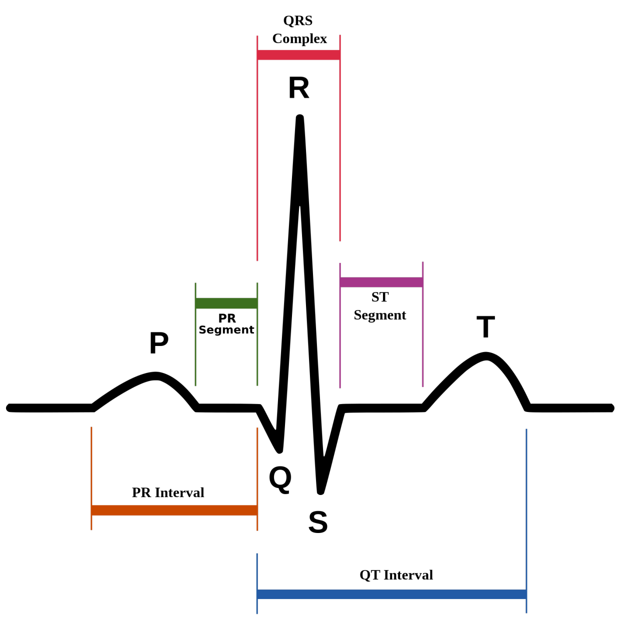


Figure 1: Partition of an ECG interval[2]

The AV-node is the junction between the atrial and ventricular impulse conduction. It therefore plays a critical role in the electrical conduction system. A dysfunction directly affects the occurrence of ventricular response.

[2] Agateller, Wikimedia Commons, URL:http://en.wikipedia.org/wiki/File:SinusRhythmLabels.png

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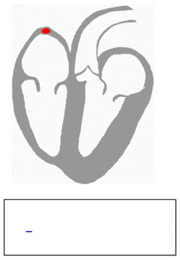
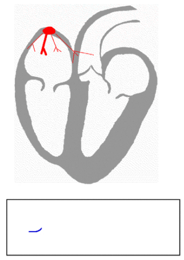
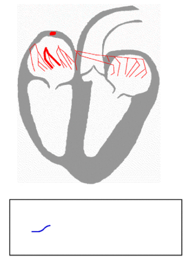
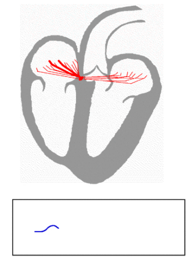
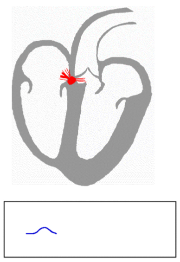
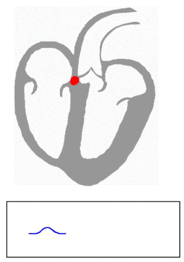
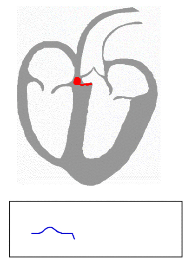
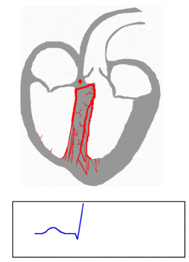
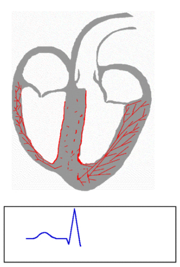
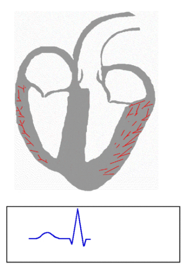
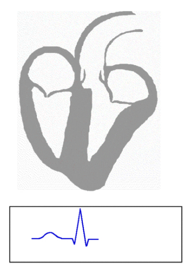
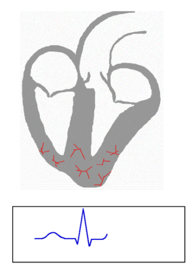
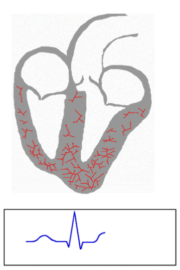
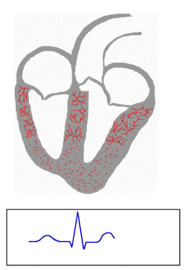
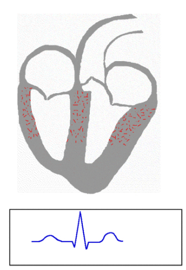
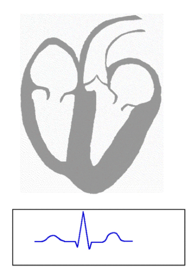
|  |  |  |  |
| Cycle begins at the sinoatrial node. | The sinus impulse is spread. | Conduction alongside the atria. | Atrial contraction. |
|  |  |  |  |
| The AV-node receives the impulse. | Short propagation delay (location of possible AV-blocks). | AV-node spreads the impulse. | Propagation through the His-bundle. Starting R-complex on the ECG. |
|  |  |  |  |
| Impulse enters the Purkinje fibers. | Beginning contraction. | Ventricles contract. | Impulse to restore resting state spreads. |
|  |  |  |  |
| Signal propagation. | Ventricular repolarization. | Ventricular repolarization. | Resting state. |

Table 1: Schematic Representation of the Cardiac Cycle[3]

[3]Kalumet, Wikimedia Commons, URL:http://commons.wikimedia.org/wiki/File:ECG_Principle_fast.gif, licensed under cc-by-sa-3.0, http://creativecommons.org/licenses/by-sa/3.0

## 2.2 AV-Blocks

In cases of atrial flutter the atrial activation is regular due to regular flutter waves. However, the conduction alongside the AV-node is disturbed. These blocks cause the irregularity in the ECG and make atrial flutter difficult to distinguish from atrial fibrillation. Mobitz and Wenckebach described such dysfunctions by observing characteristic patterns of R-R intervals in the ECG. These dysfunctions are commonly referred as second degree AV-blocks.

### Second degree AV-Block type Wenckebach

In case of an AV-block of the type Wenckebach, the propagation delay within the AV-node increases with every completed beat. If the delay exceeds a certain duration the transmitted impulse is dismissed upon receipt. This causes the cycle to reset itself and the aforementioned pattern recommences. Listing 1 explains the basic behavior of this type of AV-blocks. With every ventricular response the propagation delay increases. If the total delay oversteps a certain limit $\overline{\tau}_{ref}$, the following impulse fails. After that, the cycle resets itself. The Wenckebach-block is described by the parameters $\overline{\tau}_{con}$, $\overline{\tau}_{inc}$ and $\overline{\tau}_{ref}$[7][8][3, p. 60].

```
% set initial values for counters
b = 0;
j = 1;

% go through every incomming beat
for i=1:K
  % if possible, propagate the beat
  if(tcon + b*tinc <= tref)
    % safe the new level status
    r[j] = t[i] + tcon + b*tinc;
    b = b + 1;
    j = j + 1;
  else
    b = 0;
  end
end
```

Listing 1: Wenckebach-type AV-block

### Second degree AV-Block type Mobitz

An AV-block of the type Mobitz causes a sudden failure of ventricular response for one single input signal without previous increase of the propagation delay. This failure follows a certain pattern $(B : 1)$ meaning only every $(B+1)$th beat is successful propagated. The general behavior is described by listing 2. After passing through an input signal a refractory period $\overline{\tau}_{ref}$ is initiated. During this period the propagation of any input signal ceases. After the expiry of the refractory period the next incoming signal is propagated again and the cycle resumes. The parameters $\overline{\tau}_{con}$ and $\overline{\tau}_{ref}$ describe Mobitz-type AV-blocks[7][8][3, p. 60].

```
% set initial values for counters
b = 0;
j = 1;

% go through every incomming beat
for i=1:K
  % if possible, propagate the beat
  if(t[i] >= b)
    % safe the new level status
    r[j] = t[i] + tcon;
    b = t[i] + tref;
    j = j + 1;
  end
end
```

Listing 2: Mobitz-type AV-block

# 3 MAVBA Algorithm

The MAVBA algorithm was developed by Scholz et al. to further faciliate the distinction of atrial flutter and atrial fibrillation. The algorithm uses the length of R-R intervals[4] to uncover the source of irregular ventricular contraction.

Reconsidering the previous chapter, atrial flutter is characterized by regular atrial impulses and conduction blocks within the AV-node. This is the key difference to atrial fibrillation. For a measured set of R-R intervals the algorithm tries to emulate this given pattern. To do this, it may only use a regular input signal and two levels of AV-blocks. The overall objective is to minimize a least-squares error-function between the emulation and the measurements. A relative small objective and therefore a successful simulation indicates atrial flutter. A high objective in turn indicates atrial fibrillation.

The used multi-level AV-block consists of one Mobitz-level followed by a Wenckebach-level or vice versa. The result after passing the first block is used as the input for the second block. Each block-level is generated during runtime out of multiple sub-blocks of the corresponding block-type. Each sub-block has individual combinations of the characterizing parameters. The algorithm can adjust the combination of these modules and the input signal. This results in the following general workflow:

1. Take the measured ECG as input.
2. Determine optimal block-composition per level and input pattern to emulate the ECG as accurate as possible.

With this algorithm, based on a study with 100 patiens, 50 of whom with atrial flutter and 50 with atrial fibrillation, a high diagnostic accuracy with a sensitivity of 84% and a specificity of 74% was achieved. The highest accuracy was achieved on a time horizon containing 16 R-R intervals.

Scholz et al. cite two reasons for still existing cases of atrial flutter with a high objective value. First, the total separation in Mobitz- and Wenckebach-type AV-blocks makes it difficult to explain rare electrophysiological phenomena that need a block-structure not supported by either of the two. Second, in order to limit the amount of possible sub-blocks to a finite number, all parameters only support discrete increments [2].

An approach supporting a broader range of phenomena could help to explain more cases of atrial flutter and thereby decrease the simulation error. Furthermore, a suitable formulation could then enable the use of continuous parameters to make even more accurate predictions. The Q-model could be a first step towards formulating such a generalized approach accommodating both of the mentioned problems [2].

[4] Interval between two consecutive R-complexes on the ECG

# 4 The Q-Model

The simulation of MAVBA is based on the discrimination of a second-degree AV-block in Type I (Wenckebach) and Type II (Mobitz). The idea of the Q-model is to formulate a new approach based on a more general description of AV-blocks [7]. This model should explain both the observations of Mobitz and Wenckebach as special cases.

## 4.1 Model Definition

The core idea is to relate a degree of exhaustion $Q$ to every AV-level. An incoming impulse is only propagated if this exhaustion observes a certain limit $Q_{max}$. Otherwise, the beat is discarded. Every propagated signal lowers the potential of the level and therefore causes an increase of $Q$. Over time the level regenerates to restore its propagation-ability.

Let $s_1, ..., s_K$ be all points in time of incoming impulses and $r_1, ..., r_{n_{ECG}}$ the resulting R-complexes on the surface ECG. Listing 3 describes the general behavior of a single level simulated with the Q-Model.

```
% set initial value of Q at t = 0
Q = Q0;
j = 1;

% regenerate to first beat
Q = regenerate(Q, 0, s[1]);

% go through every incomming beat
for i=1:K
  % if possible, propagate the beat
  if(Q <= Qmax)
    % safe the new level status
    [Q, r[j]] = propagate_beat(Q, s[i]);
    j = j + 1;
  end

  if(i < K)
    % regenerate to the next beat
    Q = regenerate(Q, s[i], s[i+1]);
  end
end
```

Listing 3: General behavior of the Q-model

The function `propagate_beat` updates the state $Q$ and returns the time-point at which the R-complex occurs on the ECG. This simulates the propagation delay. This thesis is based on the assumption of a constant and an additional linear delay which depends on $Q$. The rate of regeneration $Q_{reg}$ depends linearly on the time. The resulting modifications are stated in listing 4 [7].

```
% set initial value of Q at t = 0
Q = Q0;
j = 1;

% regenerate to first beat
Q = Q - s[1] * Qreg;

% go through every incomming beat
for i=1:K
  % if possible, propagate the beat
  if(Q <= Qmax)
    % safe the new level status
    r[j] = s[i] + tcon + Q*tinc;
    Q = Q + dQ;
    j = j + 1;
  end

  if(i < K)
    % regenerate to the next beat
    Q = Q - (s[i+1] - s[i]) * Qreg;
  end
end
```

Listing 4: Q-model with linear regeneration and propagation delay

To describe the incoming impulses additional parameters are needed. It is first assumed that the pattern occurs perfectly regular. Let therefore $t_0$ be the input signal of the first impulse and $\Delta_t$ the constant time gap between two beats. In figure 2 the effect of each parameter is illustrated using a simple forward-simulation.

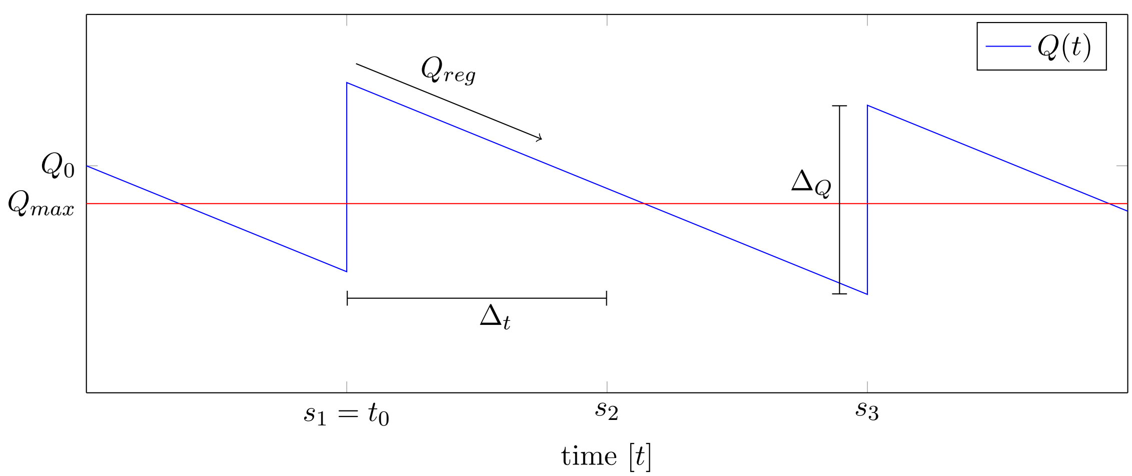



Figure 2: Q-Model Sample

### Explicit Form of $Q$

With the model-definition above, it is possible to state the trajectory $Q : \mathbb{R} \to \mathbb{R}$ of the AV-level status over the whole simulation interval. However, in order to do this, the time of every propagated impulse $t_1, \dots, t_{n_{ECG}}$ must be known over the complete time-horizon of $n_{ECG}$ successful beats. This knowledge assumed one can define an explicit notation of $Q$:

$$Q(t) = \begin{cases} Q_0 - tQ_{reg} & t \leq t_1 \\ Q_0 + (i-1)\Delta_Q - tQ_{reg} & \exists i = 1 \dots n_{ECG} : t \in (t_{i-1}, t_i] \\ Q_0 + n_{ECG}\Delta_Q - tQ_{reg} & t > t_{n_{ECG}} \end{cases} \tag{4.1}$$

In the beginning, the AV-level regenerates to the first beat at $t_1$. Then, the function enters the second definition. The cell is still regenerating but the level of exhaustion increases at every propagation by $\Delta_Q$. One can observe that the function is monotonically decreasing within every definition. This can later be used to simplify the model constraints.

## 4.2 Behavior Analysis of the Q-Model

The parameters of the Q-Model should be chosen so that the resulting simulation produces a feasible physiological pattern. While it is difficult to exactly define such valid patterns, at least definitely unfeasible cases can be excluded. Through the definition above, the Q-Model depends on the parameters $Q_0$, $Q_{reg}$, $Q_{max}$, $\Delta_Q$, $\tau_{inc}$, $\tau_{con}$, $t_0$ and $\Delta_t$. In general, the model must observe the following constraints:

1. All parameters have to be non-negative. This follows directly from the directional definition of every variable.

2. The propagation delay has to be non-negative. Hence, it must hold that

   $$Q(t_i)\tau_{inc} \geq 0 \qquad \forall i = 1 \dots n_{ECG}.$$

   Since the degree of exhaustion has a local minimum at every beat $t_i$ by definition and $\tau_{inc}$ is not negative, the function $Q$ must observe the general constraint

   $$Q(t) \geq 0 \qquad \forall t \in [0, t_{n_{ECG}}].$$

To ensure that the second constraint is observed at every point in time during the simulation multiple conditions need to be fulfilled.

### Regeneration Rate

The trajectory of $Q$ does not depend on the propagation delay and therefore only on $Q_{reg}$, $Q_{max}$, $\Delta_Q$, $Q_0$, $t_0$ and $\Delta_t$. To avoid a decrease below zero the regeneration between two incoming beats must not exceed $\Delta_Q$. If a higher rate was assumed so that $Q_{reg}\Delta_t > \Delta_Q$, the value of $Q$ would decrease between two input signal even if every beat was successful. It would then hold

$$\lim_{t \to \infty} Q(t) = -\infty$$

so that the value of $Q$ would drop below zero for a large enough time horizon. In order to avert this it must hold:

$$Q_{reg}\Delta_t \leq \Delta_Q \tag{4.2}$$

**Propagation Limit**

Assuming that $Q(t) > Q_{max}$, the level of exhaustion at the next impulse is

$$\begin{aligned} Q(t+\Delta_t) &= Q(t) - Q_{reg}\Delta_t \\ &\geq Q(t) - \Delta_Q \\ &> Q_{max} - \Delta_Q. \end{aligned}$$

To still ensure that $Q(t+\Delta_t) \geq 0$, the propagation limit $Q_{max}$ must be at least $\Delta_Q$ above zero:

$$Q_{max} \geq \Delta_Q \tag{4.3}$$

**Value-range of $Q$**

Before being able to set constraints for the start value $Q_0$, the range that $Q$ can display must be examined. This can be done by reconsidering the previous results.

- A beat is only propagated if $Q(t) \leq Q_{max}$. After that, $Q$ increases by $\Delta_Q$. Since $Q$ is monotonically decreasing in every partial definition, the function has a local maximum immediately after every propagation. It follows:

  $$Q(t) \leq Q_{max} + \Delta_Q \qquad \forall t \in [0, t_{n_{ECG}}].$$

- The regeneration rate $Q_{reg}$ is limited by the constraint (4.2). Hence, between two attempted propagations the cell restores at most $\Delta_Q$. Let $t$ be a random beat and the value $Q(t)$ be already known. There are now two cases:

  1. Let $t$ be a not propagated impulse with $Q(t) > Q_{max}$. At the next beat $t + \Delta_t$ the value of $Q$ holds

     $$\begin{aligned} Q(t+\Delta_t) &= Q(t) - \Delta_t Q_{reg} \\ &> Q_{max} - dtQ_{reg} \\ &\geq Q_{max} - \Delta_Q. \end{aligned}$$

  2. Let now be $Q(t) \leq Q_{max}$. Hence, the impulse at $t$ is propagated. Reconsidering the result (4.2), it follows

     $$\begin{aligned} Q(t+\Delta_t) &= Q(t) - \Delta_t Q_{reg} + \Delta_Q \\ &\geq Q(t) - \Delta_Q + \Delta_Q \\ &= Q(t). \end{aligned}$$

     This can then be used recursively until a previous failed impulse. The first case can then be used to also state

     $$Q(t) > Q_{max} - dQ,$$

     where $t$ is the point of time of a failed or successful propagated impulse.

  Since the function $Q$ has a local minimum at every propagated impulse $t_i$, this result can be generalized to

  $$0 \leq Q_{max} - \Delta_Q \leq Q(t) \leq Q_{max} + \Delta_Q \qquad \forall t \in [0, t_{n_{ECG}}]. \tag{4.4}$$

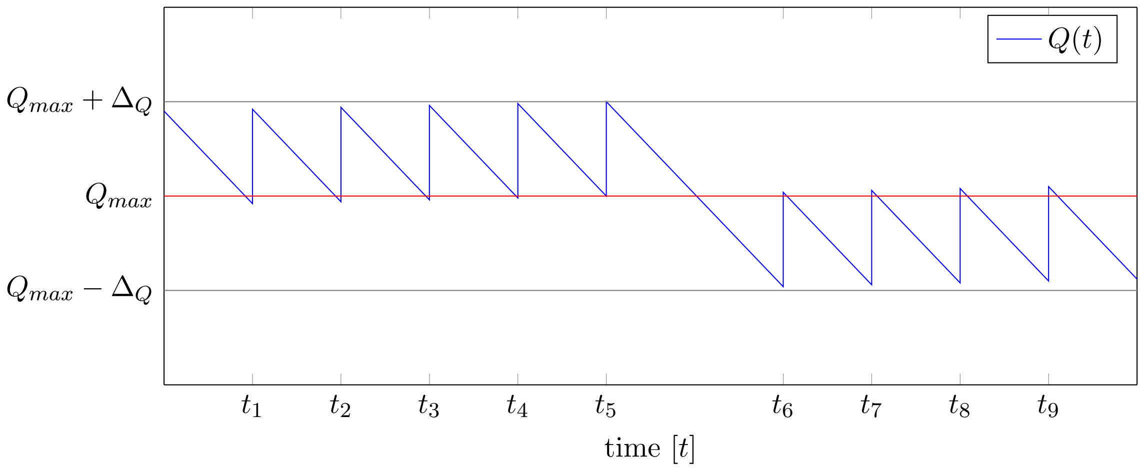



Figure 3: Trajectory Bounds of $Q$

**Initial Value $Q_0$**

The parameter $Q_0$ must ensure a behavior at the start of the simulation that observes the constraints. With the limitations above, the trajectory of $Q$ can not fall below zero once the first incoming beat at $t_0$ is reached. Hence, only the time-span $[0, t_0]$ must be observed.

- Since $Q_0$ cannot overstep the range of $Q$, it must hold:

$$Q_{max} - \Delta_Q \leq Q_0 \leq Q_{max} + \Delta_Q. \tag{4.5}$$

- Case 1: $Q(t_0) = Q_0 - t_0 Q_{reg} > Q_{max}$. With condition (4.5) and $Q_{reg} \geq 0$ it directly follows, that

$$Q_{max} - \Delta_Q < Q_{max} < Q(t_0) \leq Q_{max} + \Delta_Q.$$

  Therefore, this case is valid.

- Case 2: $Q(t_0) = Q_0 - t_0 Q_{reg} \leq Q_{max}$. The function still must not violate the constraint $Q(t_0) \geq Q_{max} - \Delta_Q$:

$$\begin{aligned} & Q(t_0) \geq Q_{max} - \Delta_Q \\ \Leftrightarrow \quad & Q_0 - t_0 Q_{reg} \geq Q_{max} - \Delta_Q \\ \Leftrightarrow \quad & Q_0 \geq Q_{max} - \Delta_Q + t_0 Q_{reg} \end{aligned} \tag{4.6}$$

The conditions (4.2), (4.3), (4.5) and (4.6) guarantee a behavior of the described AV-level, that respects the above constraints. Nonetheless, the bounds for every parameter itself still have to be chosen satisfactorily. Besides finding feasible parameter ranges, it is also desirable to reduce the overall number of optimization variables. Through structure exploitation it is possible to decrease this amount by fixing $Q_{max}$, $\Delta_Q$ and $t_0$ without loss of generality.

**Fixing $\Delta_Q$**

Let $Q(t)$ be described with known parameters and $\overline{Q} : \mathbb{R} \to \mathbb{R}$ be defined as

$$\begin{aligned}
\overline{Q}(t) :&= \frac{Q(t)}{\Delta_Q} \\
&= \begin{cases} \frac{Q_0}{\Delta_Q} - t\frac{Q_{reg}}{\Delta_Q} & t \leq t_1 \\ \frac{Q_0}{\Delta_Q} + (i-1)\frac{\Delta_Q}{\Delta_Q} - t\frac{Q_{reg}}{\Delta_Q} & \exists i = 1 \dots n_{ECG} : t \in (t_{i-1}, t_i] \\ \frac{Q_0}{\Delta_Q} + n_{ECG}\frac{\Delta_Q}{\Delta_Q} - t\frac{Q_{reg}}{\Delta_Q} & t > t_{n_{ECG}} \end{cases} \\
&= \begin{cases} \overline{Q}_0 - t\overline{Q}_{reg} & t \leq t_1 \\ \overline{Q}_0 + (i-1) - t\overline{Q}_{reg} & \exists i = 1 \dots n_{ECG} : t \in (t_{i-1}, t_i] \\ \overline{Q}_0 + n_{ECG} - t\overline{Q}_{reg} & t > t_{n_{ECG}} \end{cases}
\end{aligned}$$

By fixing the remaining parameters to

$$\begin{aligned}
\overline{Q}_{max} &:= \frac{Q_{max}}{\Delta_Q} \\
\overline{\tau}_{inc} &:= \tau_{inc}\Delta_Q \\
\overline{\tau}_{con} &:= \tau_{con},
\end{aligned}$$

the AV-level described by $\overline{Q}(t)$ has the exact same pattern and propagation delay as $Q(t)$. The first can be shown by examining the following two cases.

1. Let $t$ be the time of a silent beat:

$$\begin{aligned}
& Q(t) > Q_{max} \\
\Leftrightarrow \quad & \frac{Q(t)}{\Delta_Q} > \frac{Q_{max}}{\Delta_Q} \\
\Leftrightarrow \quad & \overline{Q}(t) > \overline{Q}_{max}
\end{aligned}$$

2. Let $t$ be the time of a propagated beat:

$$\begin{aligned}
& Q(t) \leq Q_{max} \\
\Leftrightarrow \quad & \frac{Q(t)}{\Delta_Q} \leq \frac{Q_{max}}{\Delta_Q} \\
\Leftrightarrow \quad & \overline{Q}(t) \leq \overline{Q}_{max}
\end{aligned}$$

Hence, $\overline{Q}(t)$ propagates a beat only if $Q(t)$ propagates the beat as well. Assuming such a propagated signal $t$, the resulting simulated beat $r$ occurs at

$$\begin{aligned}
r &= t + \tau_{con} + Q(t)\tau_{inc} \\
&= t + \tau_{con} + \frac{Q(t)}{\Delta_Q}\Delta_Q\tau_{inc} \\
&= t + \overline{\tau}_{con} + \overline{Q}(t)\overline{\tau}_{inc}
\end{aligned}$$

It is therefore possible to describe the exact same pattern and delay by fixing $\Delta_Q = 1$.

### Fixing $Q_{max}$

Reconsidering the constraint (4.4), one already knows that

$$Q_{max} - 1 \leq Q(t) \leq Q_{max} + 1 \qquad \forall t \in [0, t_{n_{ECG}}].$$

Thus, $Q_{max}$ has to be at least 1 to ensure that $Q(t)$ is always greater or equal to 0. Let $Q$ be a known AV-Level trajectory and $s = Q_{max} - 1$ a constant shift. As above, one can now define a new function $\overline{Q} : \mathbb{R} \to \mathbb{R}$ as

$$\begin{aligned}
\overline{Q}(t) &:= Q(t) - s \\
&= \begin{cases} (Q_0 - s) - tQ_{reg} & t \leq t_1 \\ (Q_0 - s) + (i-1) - tQ_{reg} & \exists i = 1 \ldots n_{ECG} : t \in (t_{i-1}, t_i] \\ (Q_0 - s) + n_{ECG} - tQ_{reg} & t > t_{n_{ECG}} \end{cases} \\
&= \begin{cases} \overline{Q}_0 - t\overline{Q}_{reg} \leq t_1 \\ \overline{Q}_0 + (i-1) - t\overline{Q}_{reg} & \exists i = 1 \ldots n_{ECG} : t \in (t_{i-1}, t_i] \\ \overline{Q}_0 + n_{ECG} - t\overline{Q}_{reg} & t > t_{n_{ECG}} \end{cases}
\end{aligned}$$

By also fixing

$$\begin{aligned}
\overline{Q}_{max} &= Q_{max} - s = 1 \\
Q_0 &= Q_0 - s \\
\overline{\tau}_{inc} &= \tau_{inc} \\
\overline{\tau}_{con} &= \tau_{con} + s\tau_{inc}
\end{aligned}$$

there can be again the same pattern and propagation delay obtained as with $Q$. To show the equivalent pattern, one must consider the same two cases as above:

1. Let $t$ be the time of a silent beat:

$$\begin{aligned}
& & Q(t) &> Q_{max} \\
&\Leftrightarrow & Q(t) - s &> Q_{max} - s \\
&\Leftrightarrow & \overline{Q}(t) &> \overline{Q}_{max}
\end{aligned}$$

2. Let $t$ be the time of a propagated beat:

$$\begin{aligned}
& & Q(t) &\leq Q_{max} \\
&\Leftrightarrow & Q(t) - s &\leq Q_{max} - s \\
&\Leftrightarrow & \overline{Q}(t) &\leq \overline{Q}_{max}
\end{aligned}$$

A propagated impulse then occurs at

$$\begin{aligned}
r &= t + \tau_{con} + Q(t)\tau_{inc} \\
&= t + \tau_{con} + (Q(t) - s)\tau_{inc} + s\tau_{inc} \\
&= t + \tau_{con} + s\tau_{inc} + \overline{Q}(t)\tau_{inc} \\
&= t + \overline{\tau}_{con} + \overline{Q}(t)\overline{\tau}_{inc}
\end{aligned}$$

Hence, it is also possible to fix $Q_{max}$ to 1 without a loss of generality of the simulation.

**Fixing $t_0$**

The parameter $t_0$ describes the first beat after starting the simulation. After that, every following beat occurs with a constant offset of $\Delta_t$. This initial timeshift $t_0$ can be ignored while calculating the input signals. Instead, it can be added right after the propagation. Let $t_i = t_0 + k\Delta_t$, $k \in \mathbb{N}$ be the input time of a propagated beat. One can now shift the input signal back by $t_0$ to $\bar{t}_i = +k\Delta_t$ with a new trajectory $\overline{Q} : \mathbb{R} \to \mathbb{R}$, defined as

$$\overline{Q}(t) := Q(t + t_0).$$

With $\overline{\tau}_{con} = \tau_{con} + t_0$ and $\overline{\tau}_{inc} = \tau_{inc}$, there can still be the same simulation result $r_i$ obtained:

$$\begin{aligned}
r_i &= t_i + tcon + Q(t_i)\tau_{inc} \\
&= (t_i - t_0) + (t_0 + \tau_{con}) + Q(t_i - t_0 + t_0)\tau_{inc} \\
&= \bar{t}_i + \overline{\tau}_{con} + Q(\bar{t}_i + t_0)\tau_{inc} \\
&= \bar{t}_i + \overline{\tau}_{con} + \overline{Q}(\bar{t}_i)\overline{\tau}_{inc}
\end{aligned}$$

For the new trajectory $\overline{Q}$ it holds

$$\overline{Q}(0) = Q(t_0).$$

Again, the trajectory $\overline{Q}$ can be stated explicitly as

$$\begin{aligned}
\overline{Q}(t) &= Q(t + t_0) \\
&= \begin{cases} Q_0 - (t + t_0)Q_{reg} & t + t_0 \leq t_1 \\ Q_0 + (i-1) - (t + t_0)Q_{reg} & \exists i = 1 \ldots n_{ECG} : t + t_0 \in (t_{i-1}, t_i] \\ Q_0 + n_{ECG} - (t + t_0)Q_{reg} & t + t_0 > t_{n_{ECG}} \end{cases} \\
&= \begin{cases} Q_0 - tQ_{reg} - t_0 Q_{reg} & t \leq t_1 - t_0 \\ Q_0 + (i-1) - tQ_{reg} - t_0 Q_{reg} & \exists i = 1 \ldots n_{ECG} : t \in (t_{i-1} - t_0, t_i - t_0] \\ Q_0 + n_{ECG} - tQ_{reg} - t_0 Q_{reg} & t > t_{n_{ECG}} - t_0 \end{cases} \\
&= \begin{cases} Q_0 - t_0 Q_{reg} - tQ_{reg} & t \leq \bar{t}_1 \\ Q_0 - t_0 Q_{reg} + (i-1) - tQ_{reg} & \exists i = 1 \ldots n_{ECG} : t \in \left(\bar{t}_{i-1}, \bar{t}_i\right] \\ Q_0 - t_0 Q_{reg} + n_{ECG} - tQ_{reg} & t > \bar{t}_{n_{ECG}} \end{cases} \\
&= \begin{cases} \overline{Q}_0 - (t + t_0)Q_{reg} & t \leq \bar{t}_1 \\ \overline{Q}_0 + (i-1) - tQ_{reg} & \exists i = 1 \ldots n_{ECG} : t \in \left(\bar{t}_{i-1}, \bar{t}_i\right] \\ \overline{Q}_0 + n_{ECG} - tQ_{reg} & t > \bar{t}_{n_{ECG}} \end{cases}
\end{aligned}$$

Hence, the parameter $t_0$ can simply be ignored, if the constant shift $\tau_{con}$ has a large enough value range to represent both $t_0$ and the constant propagation delay. Moreover, $\overline{Q}_0$ now equals the value at $\overline{Q}(0)$.

#### Summarizing the results

Combining all the simplifications, the simulation now only needs the parameters $Q_0$, $Q_{reg}$, $\tau_{inc}$, $\tau_{con}$ and $\Delta_t$. Those must observe the constraints (4.3), (4.2), (4.5) and (4.6):

$$\begin{aligned} Q_{reg}\Delta_t &\leq \Delta_Q \\ Q_{max} - \Delta_Q &\leq Q_0 \leq Q_{max} + \Delta_Q \\ Q_{max} - \Delta_Q + t_0 Q_{reg} &\leq Q_0. \end{aligned}$$

With $Q_{max} = \Delta_Q = 1$ and $t_0 = 0$, this results in

$$\begin{aligned} Q_{reg}\Delta_t &\leq 1 \\ 0 &\leq Q_0 \leq 2 \\ 0 &\leq Q_0. \end{aligned}$$

With these simplifications, the last constraint is redundant. Let $N : \mathbb{R}^5 \to \mathbb{R}^3$ be a constraint function with

$$N(Q_0, Q_{reg}, \tau_{inc}, \tau_{con}, \Delta_t) := \begin{pmatrix} Q_{reg}\Delta_t - 1 \\ Q_0 - 2 \\ -Q_0 \end{pmatrix}. \tag{4.7}$$

A set of parameters, that fulfills the condition

$$N(Q_0, Q_{reg}, \tau_{inc}, \tau_{con}, \Delta_t) \leq \begin{pmatrix} 0 \\ 0 \\ 0 \end{pmatrix}$$

now satisfies all the general requirements that were demanded at the beginning. Nonetheless, every parameter still needs a feasible lower- and upper bound. Let $\Omega$ be the set of all valid combinations of parameters by that meaning:

$$\Omega = \left\{ \omega = \begin{pmatrix} Q_0 \\ Q_{reg} \\ \tau_{inc} \\ \tau_{con} \\ \Delta_t \end{pmatrix} : N(\omega) \leq 0, \omega_{min} \leq \omega \leq \omega_{max} \right\}, \tag{4.8}$$

where $\omega_{min}, \omega_{max} \in \mathbb{R}^5$ describe the parameter ranges. This is the overall set of all parameter combinations which do not oppose the restrictions formulated at the beginning of this chapter.

$\Omega$ now characterizes all those parameters, over which a suitable algorithm has to find the best behavior of the AV-Level subject to a suitable objective. The next step is to combine an $\omega \in \Omega$ with the resulting simulated pattern and define such an objective. This being done, the problem can be formulated as a continuous differentiable MINLP.

## 4.3 MINLP Formulation

The algorithm described by Scholz et al. uses a least squares objective that evaluates the difference between the simulated and the measured ECG pattern. In order to perform such an evaluation, the amount of simulated propagations has to exactly correspond to the amount $n_{ECG}$ of measured beats. Let $m \in \mathbb{Z}^{n_{ECG}}$ be a vector with

$$m_i := \text{Amount of impulses since } t_{i-1} \qquad \forall i = 1, \ldots, n_{ECG}, \tag{4.9}$$

and

$$M_i := \sum_{k=1}^{i} m_k \qquad \forall i = 1, \ldots, n_{ECG}.$$

Figure 4 illustrates the definition. There have to be exactly $M_{n_{ECG}}$ simulated incoming beats in order to achieve the necessary $n_{ECG}$ propagated beats. Assuming that the vector $m$ is already known, the time of every beat $t_i$ can now be directly specified with

$$t_i = \Delta_t \left(M_i - 1\right) \tag{4.10}$$

To allow a first impulse at $t = 0$ one must decrease the sum over all $m_i$ by 1. This causes the first increase by $\Delta_t$ to vanish.

Since the exact time of every attempted and propagated beat is fixed, one can now implicitly state the behavior of the AV-level. The exhaustion $Q$ has to be below $Q_{max} = 1$ at every $t_i$ and above $Q_{max}$ at every discarded beat. In the interest of perceptibility the parameter $Q_{max}$ will still be used as symbolic variable.

$$Q\left(t_i\right) \leq Q_{max} \qquad \forall i = 1 \ldots n_{ECG} \tag{4.11}$$

$$Q\left(t_i + \Delta_t \cdot Q_{max}\right) > 1 \qquad \forall l = 1 \ldots m_i - 1, i = 0 \ldots n_{ECG} - 1 \tag{4.12}$$

These inequalities describe the constraints a trajectory $Q$ respects if its output matches the pattern of $m$. One can show later that this $m$ is in fact the only vector which satisfies all these conditions for a specific $Q$. Such an AV-Level then needs exactly $M_{n_{ECG}}$ incoming beats to propagate $n_{ECG}$ output signals.

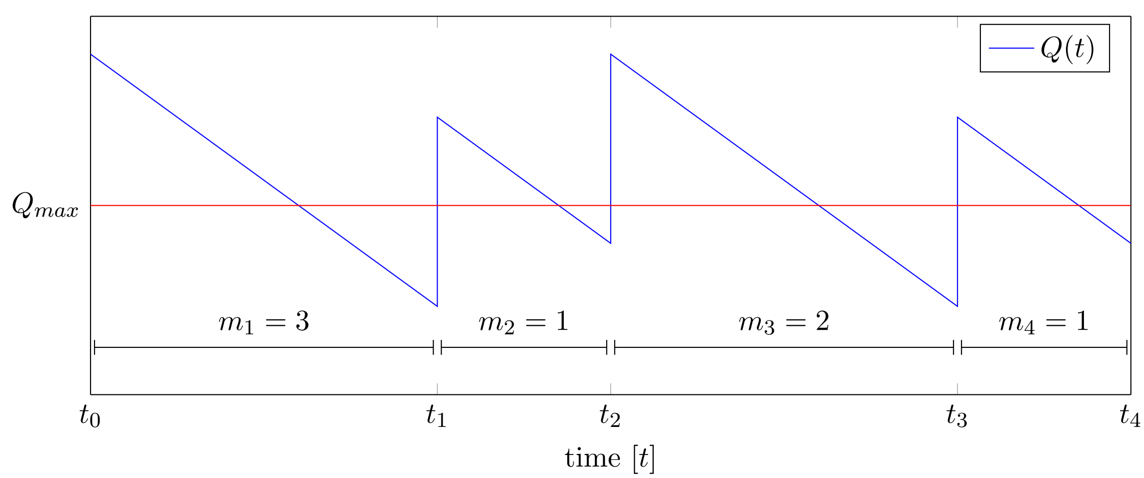



Figure 4: Pattern Representation with $m$

The function $Q$ depends on the amount of propagated beats, the time passed to regenerate and the initial value $Q_0$. Because $m$ is assumed fix, one can again directly state $Q$ at time $t$ as

$$Q(t) = \begin{cases} Q_0 - tQ_{reg} & t \leq t_1 \\ Q_0 + (i-1) - tQ_{reg} & \exists i = 1 \dots n_{ECG} : t \in (t_{i-1}, t_i] \\ Q_0 + n_{ECG} - tQ_{reg} & t > t_{n_{ECG}} \end{cases}.$$

This means for the inequalities (4.11) and (4.12)

$$\begin{aligned} Q_0 + (i-1) - t_i \cdot Q_{reg} &\leq Q_{max} & \forall i &= 1 \dots n_{ECG}, \\ Q_0 + (i-1) - (t_{i-1} + \Delta_t \cdot l) \cdot Q_{reg} &> Q_{max} & \forall l &= 1 \dots m_i - 1, \\ & & i &= 1 \dots n_{ECG}. \end{aligned}$$

Reconsidering (4.10) from above, the explicit appearance of every $t_i$ can now be vanished by replacing them with their definition:

$$\begin{aligned} Q_0 + (i-1) - (M_i - 1)\,\Delta_t Q_{reg} &\leq Q_{max} & \forall i &= 1 \dots n_{ECG} \\ Q_0 + (i-1) - (M_{i-1} - 1 + l)\,\Delta_t Q_{reg} &> Q_{max} & \forall l &= 1 \dots m_i - 1, \\ & & i &= 1 \dots n_{ECG} \end{aligned}$$

These inequalities can be placed in constraint-functions which in turn determine whether a combination $(m,\, \omega)$ results in exactly $n_{ECG}$ propagations. The Model therefore needs two types of constraints for the propagated and the silent impulses respectively.

### Constraints for propagated beats

A suitable constraint should allow only a combination $(m,\, \omega)$ which satisfies the inequalities (4.11). Let $H : \mathbb{Z}^{n_{ECG}} \times \mathbb{R}^{n_\omega} \to \mathbb{R}^{n_{ECG}}$ be the function defined as

$$\begin{aligned} H(m, \omega) :=& \begin{pmatrix} Q_0 + 0 - (M_1 - 1)\,\Delta_t Q_{reg} - Q_{max} \\ Q_0 + 1 - (M_2 - 1)\,\Delta_t Q_{reg} - Q_{max} \\ \vdots \\ Q_0 + (n_{ECG} - 1) - (M_{n_{ECG}} - 1)\,\Delta_t Q_{reg} - Q_{max} \end{pmatrix} \\ \leq& \; 0 \end{aligned}$$

If this requirement is fulfilled, every beat at $t_1, \dots, t_{n_{ECG}}$ is propagated.

### Constraints for silent beats

The vector $m$ describes the pattern of successful and failed propagations. To satisfy this pattern the trajectory $Q$ must be above $Q_{max}$ at every silent beat and therefore fulfill the strict inequalities (4.12).

The amount of constraints described by (4.12) depends on $m$. But since $Q$ is monotonically decreasing within every partial definition, this amount can be reduced to at most $n_{ECG}$ constraints of the form

$$\begin{aligned} & Q_0 + (i-1) - (t_i - \Delta_t)\, Q_{reg} > Q_{max} & \\ \Leftrightarrow \quad & Q_0 + (i-1) - (M_i - 2)\,\Delta_t Q_{reg} > Q_{max} & \text{for certain } i \in \{1, \dots, n_{ECG}\} \end{aligned}$$

This results from considering the following two cases:

1. Let $m_i$ be greater or equal to 2. There is now at least one silent beat between $t_{i-1}$ and $t_i$. Hence, there is a definitely failed propagation at $t_i - \Delta_t$. Since $Q$ is monotonically decreasing on the interval $(t_{i-1}, t_i]$, it holds

$$Q(t) \geq Q(t_i - \Delta_t) \qquad\qquad \forall t \in (t_{i-1}, t_i - \Delta_t].$$

Therefore, if $Q$ fulfills the condition

$$Q(t_i - \Delta_t) = Q_0 + (i-1) - (t_i - \Delta_t)Q_{reg} > Q_{max},$$

this also holds for every failed impulse between $t_{i-1}$ and $t_i$ that occurs before $t_i - \Delta_t$. Hence, only the last impulse between two propagations needs two be constrained.

2. Let $m_i$ be 1. In this case, the beat $t_i$ follows directly after the previous propagation at $t_{i-1}$. The condition can simply be dropped.

The index-set

$$I := \{i : i \in [1, \ldots, n_{ECG}], m_i \geq 2\} = \{i_1, \ldots, i_{|I|}\}$$

indicates which inequalities need to be active. Let then $J_I : \mathbb{Z}^{n_{ECG}} \times \mathbb{R}^{n_\omega} \to \mathbb{R}^{|I|}$ be the function describing the strict inequality:

$$J_I(m, \omega) = \begin{pmatrix} Q_0 + (i_1 - 1) - (M_{i_1} - 2)\,\Delta_t Q_{reg} - Q_{max} \\ Q_0 + (i_2 - 1) - (M_{i_2} - 2)\,\Delta_t Q_{reg} - Q_{max} \\ \vdots \\ Q_0 + (i_{|I|} - 1) - \left(M_{i_{|I|}} - 2\right)\Delta_t Q_{reg} - Q_{max} \end{pmatrix} > 0,$$

Fulfilling this condition, the trajectory $Q$ is forced to be above the propagation limit $Q_{max}$ at every failed impulse. This ensures that there does not exist any additional propagation besides the intentional $t_1, \ldots, t_{n_{ECG}}$. For the sake of simplicity, the representation of $J$ using $I$ will be used for the problem formulation. However, later in chapter 6.1 this will be dissolved in order to implement the resulting optimization problem.

### Combining both constraints

If $Q$ respects all the constraints demanded in (4.11) and (4.12), the AV-level generates the corresponding pattern $m$. Using $H$ and $J_I$, one can now abstract this property by joining the results from above.

**Lemma 4.1.** *Let $(m,\ \omega) \in \mathbb{Z}^{n_{ECG}} \times \Omega$ be chosen such that $H(m, \omega) \leq 0$ and $J_I(m, \omega) > 0$. Then the AV-level and the input signal, both determined by $\omega$, generates the unique pattern $m$ to simulate the first $n_{ECG}$ propagations.*

*Proof.* If the parameters $\omega \in \Omega$ are fixed, the corresponding AV-level and the input signal are uniquely determined. This can easily be proved by a simple forward-simulation of the Q-model using the chosen parameters since this is an unique process.

Assuming this simulation would have proceeded long enough, the pattern $m$, which is generated within the time-horizon of the first $n_{ECG}$ beats, is also uniquely determined. The constraints $H(m, \omega) \leq 0$ and $J_I(m, \omega) > 0$ are only then true if the value of $Q$ is below or equal to 1 at every successful and above 1 at every failed beat. Therefore, both conditions are fulfilled for the fixed $\omega$ and the generated $m$.

On the other hand, these conditions are only fulfilled if $m$ is in fact the pattern simulated by using $\omega$. Let $\bar{m}$ be a pattern that fulfills both constraints but is not equal to the actual pattern $m$ generated by an explicit simulation. With both patterns, a set of beats $t_1, \ldots, t_{n_{ECG}}$ and $\bar{t}_1, \ldots, \bar{t}_{n_{ECG}}$ is characterized. These are the first $n_{ECG}$ beats that are passed through the AV-block. There is at least one $i$ with $t_i \neq \bar{t}_i$. Since both $m$ and $\bar{m}$ fulfill the constraints $H$ and $J_I$ with $\omega$, this beat must satisfy both of these conditions. Therefore, it must hold

$$\begin{array}{lcl} Q(t_i) \leq 1 & \wedge & Q(t_i) > 1 \\ Q(\bar{t}_i) \leq 1 & \wedge & Q(\bar{t}_i) > 1 \end{array}$$

since a failed impulse occurs at $t_i$ in $\bar{m}$ and at $\bar{t}_i$ in $m$. Hence, assuming such another $\bar{m}$ leads to a conflict.

Using a fixed $\omega$, the only pattern $m$ that fulfills $H(m, \omega) \leq 0$ and $J_I(m, \omega) > 0$ is the one generated by a simple forward-simulation of the AV-level. Therefore, if $m$ and $\omega$ do satisfy these conditions, $m$ must be the actual simulation pattern. □

With this lemma it is possible to check whether a combination $(m, \omega)$ results in the desired amount of output beats without an explicit simulation. On top of that, if a valid combination is known, all the $t_i$ and therefore the complete trajectory $Q$ is also evaluable over the complete time horizon of the simulation.

### Formulating the Objective

Assuming known $m$ and $\omega$, which satisfy lemma (4.1), every point in time $t_i$ is determined. In order to evaluate the simulation as a least squares problem, the final ECG time-points $r_i$ must be calculated. A certain simulated ECG signal depends on $t_i$, the cell status $Q(t_i)$ and the propagation delay, such as

$$r_i = t_i + \tau_{con} + \tau_{inc} Q(t_i) \qquad \forall i = 1, \ldots, n_{ECG}.$$

Since all these parameters are known and the trajectory $Q$ can be evaluated, a function can be defined which returns the vector of all $r_i$, depending only on $m$ and $\omega$. Let therefore $S : \mathbb{Z}^{n_{ECG}} \times \mathbb{R}^{n_\omega} \to \mathbb{R}^{n_{ECG}}$ be defined as

$$S(m, \omega) = \begin{pmatrix} t_1 + \tau_{con} + \tau_{inc} Q(t_1) \\ t_2 + \tau_{con} + \tau_{inc} Q(t_2) \\ \vdots \\ t_{n_{ECG}} + \tau_{con} + \tau_{inc} Q(t_{n_{ECG}}) \end{pmatrix}.$$

The vector $r = S(m, \omega)$ contains the final simulation result. As above, the value of $Q(t)$ and $t_i$ can be stated explicitly:

$$
\begin{aligned}
S(m,\omega) &= \begin{pmatrix} t_1 + \tau_{con} + \tau_{inc}(Q_0 + 0 - t_1 Q_{reg}) \\ t_2 + \tau_{con} + \tau_{inc}(Q_0 + 1 - t_2 Q_{reg}) \\ \vdots \\ t_{n_{ECG}} + \tau_{con} + \tau_{inc}(Q_0 + (n_{ECG} - 1) - t_{n_{ECG}} Q_{reg}) \end{pmatrix} \\
&= \begin{pmatrix} t_1(Q_{reg}\tau_{inc} + 1) + \tau_{con} + \tau_{inc}(Q_0 + 0) \\ t_2(Q_{reg}\tau_{inc} + 1) + \tau_{con} + \tau_{inc}(Q_0 + 1) \\ \vdots \\ t_{n_{ECG}}(Q_{reg}\tau_{inc} + 1) + \tau_{con} + \tau_{inc}(Q_0 + n_{ECG} - 1) \end{pmatrix} \\
&= \begin{pmatrix} \Delta_t(M_1 - 1)(Q_{reg}\tau_{inc} + 1) + \tau_{con} + \tau_{inc}(Q_0 + 0) \\ \Delta_t(M_2 - 1)(Q_{reg}\tau_{inc} + 1) + \tau_{con} + \tau_{inc}(Q_0 + 1) \\ \vdots \\ \Delta_t(M_{n_{ECG}} - 1)(Q_{reg}\tau_{inc} + 1) + \tau_{con} + \tau_{inc}(Q_0 + n_{ECG} - 1) \end{pmatrix}
\end{aligned}
$$

**Formulating the MINLP**

Considering the previous results, the following components are now known:

- The set of all possible parameters $\omega \in \Omega$ that lead to a general feasible behavior.
- The constraints $H$ and $J_I$ which determine if a specific $\omega$ needs the pattern $m \in \mathbb{Z}^{n_{ECG}}$ to simulate exactly $n_{ECG}$ beats.
- The function $S$, which determines all $n_{ECG}$ time-points $r_i$ of the generated R-complexes.

Combining these components, a mixed-integer, non-linear optimization problem can be formulated:

$$
\begin{aligned}
\min_{m,\omega} \quad & \|S(m,\omega) - ECG\|_2 \\
\text{s.t.} \quad & H(m,\omega) \leq 0 \\
& J_I(m,\omega) > 0 \\
& m \in \mathbb{Z}^{n_{ECG}} \\
& \omega \in \Omega
\end{aligned}
\tag{4.13}
$$

This problem formulation avoids any explicit simulation of the AV-level. Using a suitable solving algorithm, the best choice of $\omega$ can be found for the underlying Q-model.

## 4.4 Emulating Mobitz and Wenckebach AV-Blocks

Reconsidering chapter 3, two problems were mentioned by Scholz et al. that probably still limit the diagnostic accuracy of their algorithm. First, the strict separation in Mobitz- and Wenckebach-type blocks makes it difficult to describe rare phenomena. Second, the discrete parameter step size limits the scope of the simulation. Using a suitable algorithm, the formulation of MINLP (4.13) makes it possible to find the best choice for $m$ and $\omega$ without actually simulating the explicit Q-model. This allows the use of continuous parameters. Thus, the second limitation is eliminated.

The approach of the Q-model is more general then a strict decision between Mobitz and Wenckebach. Furthermore, it can be shown that these two types of AV-blocks are in fact just special cases within all possible simulations and can therefore be emulated by the Q-model.

Certainly, this does not state an explicit relation between MAVBA and the Q-model since Scholz et at. build their blocks out of multiple block-modules. Nonetheless, this new approach is capable of imitating the basic sub-blocks that MAVBA uses. Therefore, both algorithms have a common intersection of possible simulations.

### Emulating a Mobitz-block

As discussed in chapter 2.2, a Mobitz-type block satisfies a (B:1) pattern, meaning that only every (B+1)th input signal excites a ventricular response. Using suitable parameters, the Q -model is able to emulate the same behavior as a strict Mobitz-type AV-block.

**Lemma 4.2.** *For every B:1 Mobitz-pattern exists a combination* $(m, \omega)$ *with* $H(m, \omega) \leq 0$ *and* $J(m, \omega) > 0$ *that emulates the behavior of the Mobitz AV-level.*

*Proof.* Let $t_1$ and $t_2$ be the time points of a first and a second propagated beat. The Mobitz-pattern repeats after every propagated beat. If one can show that the Q-Model simulation behaves like the given Mobitz AV-block and it also holds $Q(t_1) = Q(t_2)$, the Q-Model has to emulate the Mobitz-pattern for every time-interval.

For the sake of simplicity, let the timespan of the simulation be shifted so that $t_1 = 0$. This can be done without a loss of generality, by adjusting $Q_0$ and $m_1$. Therefore, it holds $Q(t_1) = Q_0$. The second beats occurs after $B$ discarded beats. This results in the pattern $m = (1, B+1)$ for the Q-level.

Since it is demanded that $Q(t_1) = Q(t_2)$, one arrives at

$$\begin{aligned}
& Q(t_1) = Q(t_2) \\
\Leftrightarrow \quad & Q_0 = Q_0 + 1 - (B+1)\Delta_t Q_{reg} \\
\Leftrightarrow \quad & 0 = 1 - (B+1)\Delta_t Q_{reg} \\
\Leftrightarrow \quad & (B+1)\Delta_t Q_{reg} = 1 \\
\Leftrightarrow \quad & \Delta_t Q_{reg} = \frac{1}{B+1} \qquad (4.14)
\end{aligned}$$

With this fixed pattern, also the total regeneration between two received impulses must be fixed.

To ensure that the beats $t_1$ and $t_2$ actually are propagated it must hold:

$$\begin{aligned}
H(m,\omega) &= \begin{pmatrix} Q_0 + (M_1 - 1)\Delta_t Q_{reg} - 1 \\ Q_0 + 1 - (M_2 - 1)\Delta_t Q_{reg} - 1 \end{pmatrix} \\
&= \begin{pmatrix} Q_0 - 1 \\ Q_0 - (B+1)\Delta_t Q_{reg} \end{pmatrix} \\
&= \begin{pmatrix} Q_0 - 1 \\ Q_0 - \frac{B+1}{B+1} \end{pmatrix} \\
&= \begin{pmatrix} Q_0 - 1 \\ Q_0 - 1 \end{pmatrix} \\
&\leq 0
\end{aligned}$$

Hence, if $Q(t_1) = Q_0$ is below or equal to $Q_{max} = 1$, all necessary impulses get successfully propagated.

In order to prevent any additional propagation, the second constraint must also be respected. Since $m_1 = 1$, there are only two possibilities for the necessary index-set I:

1. $B \geq 1$ and $m_2 \geq 2$. For the index set, this means:

   $$I = \{2\}.$$

   The corresponding constraint then is

   $$\begin{aligned}
   J_I(m,\omega) &= Q_0 + (2-1) - (M_2 - 2)\Delta_t Q_{reg} - 1 \\
   &= Q_0 + 1 - \frac{B}{B+1} - 1 \\
   &= Q_0 - \frac{B}{B+1} > 0.
   \end{aligned}$$

   With this, it directly follows

   $$Q_0 > \frac{B}{B+1}$$

   Combining this and the previous result $Q_0 \leq 1$ the valid range for $Q_0$ can be stated:

   $$Q_0 = Q(t_1) \in \left(\frac{B}{B+1}, 1\right] \tag{4.15}$$

   If such a $Q_0$ is chosen, both $H(m,\omega) \leq 0$ and $J_I(,\omega) > 0$ are satisfied.

2. $B = 0$ and therefore $m_2 = 1$. In this case, it holds

   $$I = \emptyset.$$

   Hence, $Q_0$ can be chosen freely within the range

   $$Q_0 = Q(t_1) \in (0,1] = \left(\frac{B}{B+1}, 1\right].$$

It is therefore always possible to find suitable parameters for the Q-Model to match the pattern of a general 1:B Mobitz block.

A Mobitz-level only has a constant propagation delay $\tau_{con,M}$. The delay of the Q-model must equal this constant shift, to simulate the exact same behavior as a Mobitz block. Since the value of $Q$ is constant at every propagated beat with $Q(t_1) = Q(t_2) = Q_0$, one must only look at the first propagation at $t_1$. The delay of the Q-model must hold

$$\tau_{con} + Q(t_1)\tau_{inc} = \tau_{con,M}. \tag{4.16}$$

Hence, if the conditions (4.14), (4.15) and (4.16) are fulfilled, the AV-block, described by the Q-model and the underlying parameters $\omega$, emulates the exact same behavior of an 1:b Mobitz block. $\square$

This result can be used, to declare additional model constraints for the MINLP (4.13). This new conditions then force the Q-model to simulate a Mobitz block. Due to the proof of lemma (4.2) the following constraints need to be added:

$$\begin{aligned} Q(t_1) - 1 &\leq 0 \\ Q(t_1) - \frac{B}{B+1} &> 0 \\ \Delta_t Q_{reg} - \frac{1}{B+1} &= 0 \end{aligned}$$

As shown in the proof above, the condition for the product $\Delta_t Q_{reg}$ forces the value of $Q$ to be identical at every beat $t_1, \ldots, t_{n_{ECG}}$. Therefore, only one beat, in this case the first, must be observed. Moreover, such a chose of $Q(t_1)$ ensures that the conditions $H(m, \omega) \leq 0$ and $J_I(m, \omega) > 0$ are satisfied. This is why the trajectory only needs to be evaluated at $t_1$:

$$\begin{aligned} Q(t_1) &= Q_0 - t_1 Q_{reg} \\ &= Q_0 - (m_1 - 1)\Delta_t Q_{reg} \\ &= Q_0 - (m_1 - 1)\frac{1}{B+1} \end{aligned}$$

If the value of $m_1$ and the Mobitz pattern $1 : B$ is known, every further $m_i$ is determined by those two parameters. Hence, the overall number of integer variables can be fixed to only these these two. For any $m_i$, it now holds

$$m_i = B + 1 \qquad \forall i \in \{2, \ldots, n_{ECG}\},$$

and therefore

$$t_i = (m_1 + (i-1)(B+1) - 1)\Delta_t \qquad \forall i \in \{1, \ldots, n_{ECG}\}$$

If the delay of the desired Mobitz-block is already known, it is also needed to constraint the delay with

$$\tau_{con} + Q(t_1)\tau_{inc} - \tau_{con,M} = 0.$$

Either way, the delay is always constant since the value of $Q$ is constant at every propagation. Therefore only a constant delay parameter is needed and $\tau_{inc}$ can be ignored if $\tau_{con}$ has been chosen suitable.

The function $S$ can now also be simplified by just depending on $m_1$, $B$ and $\omega$. Let $S : \mathbb{Z}^2 \times \mathbb{R}^{n_\omega} \to \mathbb{R}^{n_{ECG}}$ be defined as

$$
\begin{aligned}
S(m_1, B, \omega) &= \begin{pmatrix} t_1 + \tau_{con} \\ t_2 + \tau_{con} \\ \vdots \\ t_{n_{ECG}} + \tau_{con} \end{pmatrix} \\
&= \begin{pmatrix} (m_1 - 1)\Delta_t + \tau_{con} \\ (m_1 + (B+1) - 1)\Delta_t + \tau_{con} \\ \vdots \\ (m_1 + (n_{ECG} - 1)(B+1) - 1)\Delta_t + \tau_{con} \end{pmatrix} \\
&= \begin{pmatrix} (m_1 - 1)\frac{1}{Q_{reg}(B+1)} + \tau_{con} \\ (m_1 + (B+1) - 1)\frac{1}{Q_{reg}(B+1)} + \tau_{con} \\ \vdots \\ (m_1 + (n_{ECG} - 1)(B+1) - 1)\frac{1}{Q_{reg}(B+1)} + \tau_{con} \end{pmatrix}.
\end{aligned}
$$

The last transformation uses

$$
\begin{aligned}
& \Delta_t Q_{reg} - \frac{1}{B+1} = 0 \\
\Leftrightarrow \quad & \Delta_t = \frac{1}{Q_{reg}(B+1)}.
\end{aligned}
$$

The parameter $\Delta_t$ is only used implicitly, both within the constraints and the objective. Hence, it can be excluded from $\omega$, which at this point only contains the parameters $Q_0$, $Q_{reg}$ and $\tau_{con}$. The set $\Omega$ can be simplified to

$$
\Omega := \left\{ \omega = \begin{pmatrix} Q_0 \\ Q_{reg} \\ \tau_{con} \end{pmatrix} : \omega_{min} \le \omega \le \omega_{max} \right\}. \tag{4.17}
$$

The set of all possible $\omega$ is now only characterized by the value limits $\omega_{min}$ and $\omega_{max}$. Using the new definition of $S$, a MINLP can be formulated:

$$
\begin{aligned}
\min_{m_1, B, \omega} \quad & \| S(m_1, B, \omega) - ECG \|_2 \\
\text{s.t.} \quad & Q_0 - (m_1 - 1)\frac{1}{B+1} - 1 && \le 0 \\
& Q_0 - (m_1 - 1)\frac{1}{B+1} - \frac{B}{B+1} && > 0 \\
& (\tau_{con} = \tau_{con,M}) \\
& m_1, B \in \mathbb{Z} \\
& \omega \in \Omega
\end{aligned} \tag{4.18}
$$

This modification of the MINLP (4.13) forces the Q-model to emulate an 1:B Mobitz block. Through structure exploitation the overall amount of optimization variables is reduced to only 5, including the two integer variables.

### Emulating a Wenckebach-block

Reconsidering again chapter 2.2, a Wenckebach-type AV-block is characterized by a linear increasing propagation delay $\overline{\tau}_{con} + b\overline{\tau}_{inc}$ with every successful beat. If a certain propagation limit $\overline{\tau}_{ref}$ is overstepped, the next impulse is dismissed and the cycle resets itself. Despite this increasing propagation delay, every so defined Wenckebach-block can again be emulated by the Q-Model.

**Lemma 4.3.** *For every Wenckebach-type AV-block exists a combination $(m, \omega)$ with $H(m, \omega) \leq 0$ and $J(m, \omega) > 0$ that emulates the behavior of the Wenckebach AV-level.*

*Proof.* First, the regular input for the Q-model should be the same as the Wenckeback-levels input. Therefore, the parameter $\Delta_t$ is fixed.

Since the parameters $\overline{\tau}_{con}$, $\overline{\tau}_{inc}$ and $\overline{\tau}_{ref}$ are known, the general pattern of the AV-block can be specified. An impulse only is propagated if the condition

$$\overline{\tau}_{con} + b\overline{\tau}_{inc} \leq \overline{\tau}_{ref}$$

is respected. Let $B$ be the first beat that violates this constraint. It holds

$$\begin{aligned} \overline{\tau}_{con} + b\overline{\tau}_{inc} &\leq \overline{\tau}_{ref} && \forall b = 0, \dots, B-1 \\ \overline{\tau}_{con} + B\overline{\tau}_{inc} &> \overline{\tau}_{ref}. \end{aligned}$$

After the impulse is dismissed, the Wenckebach-level resets. Therefore, this $B:1$-pattern consists of $B$ propagations followed by one silent beat.

Let $t_1, \dots, t_B$ be the points in time of the successful impulses and $t_{B+1}$ the failed one. The pattern restarts at $t_{B+2}$. As already shown, it can be assumed that $t_1 = 0$ and therefore $Q(t_1) = Q_0$ without loss of generality. This results in a pattern $m \in \mathbb{Z}^{B+1}$, with

$$m = (1, \dots, 1, 2).$$

To ensure that this pattern repeats itself, it must hold:

$$\begin{aligned} & Q(t_1) = Q(t_{B+2}) \\ \Leftrightarrow \quad & Q_0 = Q_0 - (B+1)\Delta_t Q_{reg} + B \\ \Leftrightarrow \quad & \Delta_t Q_{reg} = \frac{B}{B+1} < 1 \end{aligned} \tag{4.19}$$

The regeneration rate per beat is fixed by the number of successfully propagated impulses. This beats only occur if it holds $H(m, \omega) \leq 0$ and therefore

$$H(m, \omega) = \begin{pmatrix} Q(t_1) - 1 \\ \vdots \\ Q(t_B) - 1 \end{pmatrix} \leq 0$$

Every beat immediately follows the previous one. Since the regeneration rate per beat $\Delta_t Q_{reg}$ is strict smaller than $\Delta_Q = 1$, it holds

$$\begin{aligned} & Q(t_1) < Q(t_2) < \cdots < Q(t_B) \\ \Rightarrow \quad & Q(t_1) - 1 < Q(t_2) - 1 < \cdots < Q(t_B) - 1. \end{aligned}$$

One therefore must only ensure that the value of $Q$ at the last beat is below $Q_{max}$ to satisfy the constraint $H$.

$$\begin{aligned} & Q(t_B) - 1 \leq 0 \\ \Leftrightarrow \quad & Q_0 - (B-1)\Delta_t Q_{reg} + (B-1) - 1 \leq 0 \\ \Leftrightarrow \quad & Q_0 - (B-1)\Delta_t Q_{reg} + B - 2 \leq 0 \\ \Leftrightarrow \quad & Q_0 - \frac{(B-1)B}{B+1} + B - 2 \leq 0 \\ \Leftrightarrow \quad & Q_0 \leq \frac{(B-1)B}{B+1} - B + 2 \\ \Leftrightarrow \quad & Q_0 \leq \frac{2}{B+1}. \end{aligned}$$

With the fixed regeneration per beat, the initial value of $Q$ must not exceed the limit of $\frac{2}{B+1}$ in order to allow every beat $t_1, \ldots, t_B$ to get propagated. At the same time, the value of $Q$ at the dismissed beat at $t_{B+1}$ must be above $Q_{max}$ and therefore it must hold

$$J_I(m, \omega) = Q(t_{B+1}) - 1 > 0.$$

Using the definition of $Q$, one gets

$$\begin{aligned} & Q(t_{B+1}) - 1 > 0 \\ \Leftrightarrow \quad & Q_0 - B\Delta_t Q_{reg} + B - 1 > 0 \\ \Leftrightarrow \quad & Q_0 - \frac{B^2}{B+1} + B - 1 > 0 \\ \Leftrightarrow \quad & Q_0 > \frac{B^2}{B+1} - B + 1 \\ \Leftrightarrow \quad & Q_0 > \frac{1}{B+1}. \end{aligned}$$

Combining these two bounds, it must hold

$$Q_0 \in \left( \frac{1}{B+1}, \frac{2}{B+1} \right]. \tag{4.20}$$

If conditions (4.19) and (4.20) are fulfilled, both constraints $H(m, \omega) \leq 0$ and $J_I(m, \omega) > 0$ are satisfied and therefore the Q-level described by $\omega$ results in the desired pattern $m$.

In addition to this, the simulation must also match the propagation delay of the Wenckebach-type AV-block:

$$\begin{aligned} \tau_{con} + Q(t_1)\tau_{inc} &= \overline{\tau}_{con} \\ \tau_{con} + Q(t_2)\tau_{inc} &= \overline{\tau}_{con} + \overline{\tau}_{inc} \\ &\vdots \\ \tau_{con} + Q(t_B)\tau_{inc} &= \overline{\tau}_{con} + (B-1)\overline{\tau}_{inc} \end{aligned} \tag{4.21}$$

In order to fulfill this equation, the propagation delay must increase by $\overline{\tau}_{inc}$ with every beat:

$$
\begin{aligned}
& & (\tau_{con} + Q(t_i)\tau_{inc}) - (\tau_{con} + Q(t_{i-1})\tau_{inc}) &= \overline{\tau}_{inc} & \forall i = 2, \dots, B \\
&\Leftrightarrow & (Q(t_i) - Q(t_{i-1}))\tau_{inc} &= \overline{\tau}_{inc} & \forall i = 2, \dots, B \\
&\Leftrightarrow & (1 - \Delta_t Q_{reg})\tau_{inc} &= \overline{\tau}_{inc} \\
&\Leftrightarrow & (1 - \frac{B}{B+1})\tau_{inc} &= \overline{\tau}_{inc} \\
&\Leftrightarrow & \frac{1}{B+1}\tau_{inc} &= \overline{\tau}_{inc} \\
&\Leftrightarrow & \tau_{inc} &= (B+1)\overline{\tau}_{inc}
\end{aligned}
$$

Due to the fixed $\Delta_t Q_{reg}$, the linear propagation increase $\tau_{inc}$ is also fixed. This ensures an increase of the delay by $\overline{\tau}_{inc}$ with every successful impulse. To also ensure the same value, the initial delay at $t_1$ must also be equal to the delay of the first beat in the Wenckebach-block.

Using the now fixed $\tau_{con}$ in the condition (4.21), one arrives at

$$
\begin{aligned}
& & \tau_{con} + Q(t_1)\tau_{inc} &= \overline{\tau}_{con} \\
&\Leftrightarrow & \tau_{con} + Q(t_1)(B+1)\overline{\tau}_{inc} &= \overline{\tau}_{con} \\
&\Leftrightarrow & \tau_{con} &= \overline{\tau}_{con} - Q(t_1)(B+1)\overline{\tau}_{inc}
\end{aligned}
$$

By fixing both parameters $\tau_{con}$ and $\tau_{inc}$ in this way, the Q-model also has the exact same propagation delay as the initial Wenckebach-type AV-block.

Combining both results, one can emulate the pattern as well as the propagation behavior of such Wenckebach-levels. $\square$

# 5 Extending the Model

Up to this point, the Q-model proved to be capable of emulating Mobitz- as well as Wenckebach-type AV-blocks. As a result, every specific case of an AV-block, which can be described by either phenomenon, can also be explained by the Q-model. Unfortunately, this relation between both approaches so far only holds for a single level AV-block and requires perfectly equidistant input signals.

Due to the usually non-constant pattern of the simulated ECG, this requirement renders it impossible to set more than one Q-level in a row. In order to allow the simulation of AV-blocks consisting of multiple levels, the constraint that ensures constant distances between incoming impulses must be relaxed.

Since the condition of perfectly equidistant input signals is not always observed even in cases of atrial flutter, allowing small variations in the input could also improve the quality of an algorithmically generated pattern.

## 5.1 Interval Extension

So far, the input signal was characterized only by $\Delta_t$. Overall, $M_{n_{ECG}}$ impulses were needed to simulate $n_{ECG}$ successful beats. Let $s_1, \ldots, s_{M_{n_{ECG}}}$ be all of these impulses. To support varying distances between these $s_j$ the parameter $\Delta_t$ must be replaced by

$$\Delta_{t,j} \in [\Delta_{tmin}, \Delta_{tmax}] \qquad \forall j = 1, \ldots, n_{ECG} - 1.$$

The parameter $\Delta_{t,j}$ should then describe the distance between $s_j$ and $s_{j+1}$:

$$\Delta_{t,j} = s_{j+1} - s_j \qquad \forall j = 1, \ldots, n_{ECG} - 1.$$

Assuming that the vector $m$ and every $\Delta_{t,j}$ are known, all successful beats $t_1, \ldots, t_{n_{ECG}}$ are exactly determined. This pattern then has the following important characteristics.

1. Every beat $t_i$ is propagated. Therefore, it holds

$$Q(t_i) \leq 1 \qquad \forall i = 1, \ldots, n_{ECG}.$$

2. Every beat between those propagations is silent:

$$Q(s_j) > 1 \qquad \forall j = 1, \ldots, M_{n_{ECG}} \text{ and } s_j \neq t_1, \ldots, t_{n_{ECG}}.$$

Since $Q$ is still monotonically decreasing between two beats, this condition can be reduced to only the last failed beat before every propagation.

$$Q(t_i - \Delta_{t_i}) > 1 \qquad \forall i \in I,$$

where $\Delta_{t_i}$ is the distance between $t_i$ and the previous attempted beat. $I$ is again the set of every successful propagation with a previous silent beat:

$$I := \{i = 1, \ldots, n_{ECG} | m_i > 1\}.$$

If these constraints are satisfied, the AV-Level only let the necessary $n_{ECG}$ beats pass. The evaluation of these conditions depends on $Q$, the $t_i$ and the corresponding $\Delta_{t_i}$. Unfortunately, both the $t_i$ and $\Delta_{t_i}$ can occur in certain intervals due to the introduced variations in the impulse distance. They are therefore not uniquely determined by $m$ and $\omega$. Rather, they must now also be added as optimization variables. Let $t, \Delta \in \mathbb{R}^{n_{ECG}}$ be vectors containing these new variables as

$$\begin{aligned} t &:= (t_1, \dots, t_{n_{ECG}}) \\ \Delta &:= (\Delta_{t_1}, \dots, \Delta_{t_{n_{ECG}}}). \end{aligned}$$

Before setting up new constraints for these variables, the set of all possible model parameters must first be reformulated. The set of model parameters increases by $\Delta_{tmin}$ and $\Delta_{tmax}$, replacing $\Delta_t$. To use this non-constant distances within the simulation, the set $\Omega$ must be updated to support this new variables.

**Updating $\Omega$**

The previous used $\Delta_t$ in $\Omega$ is is replaced by the two parameters $\Delta_{tmin}$ and $\Delta_{tmax}$ determining the range, in which the a new attempted beat occurs. It must hold

$$\Delta_{tmin} \leq \Delta_{tmax}. \tag{5.1}$$

Since these two new parameters describe an important part of the input pattern, simply stating the relation between $\Delta_{tmin}$ and $\Delta_{tmax}$ is insufficient. All previous characteristics established to initially define $\Omega$, must be reconsidered:

1. All parameters have to be non-negative.

2. The propagation delay has to be non-negative. Since the degree of exhaustion has a local minimum at every beat $t_i$ by definition and $\tau_{inc}$ is not negative, the function $Q$ must hold the general constraint

$$Q(t) \geq 0 \qquad\qquad \forall t \in [0, t_{n_{ECG}}].$$

This behavior has been ensured by using the following constraints:

$$\begin{aligned} Q_{reg}\Delta_t &\leq \Delta_Q = 1 \\ 0 \leq Q_0 &\leq 2. \end{aligned}$$

Reconsidering the chapter 4.2, this forces the trajectory of the Q-model to only use the image range $[0, 2]$ and therefore ensure a positive propagation delay. The first constraint must be replaced by a new one using the new definition of the input signal distance.

The constraint ensures that between two impulses there can be restored at most the potential of one beat can be restored. If this condition is violated, the value of $Q$ would step below 0 at some point even if there is a propagated beat caused by every input signal. To limit the maximum regeneration rate per beat and prevent such a decrease, it must hold

$$Q_{reg}\Delta_{t,j} \leq 1 \qquad\qquad \forall j = 1, \dots, n_{ECG} - 1.$$

Since every $\Delta_{t,j}$ is within $[\Delta_{tmin}, \Delta_{tmax}]$, a single constraint can ensure this behavior, with

$$Q_{reg}\Delta_{tmax} \leq 1.$$

To therefore describe the needed relation between all parameters to describe the new $\Omega$, the constraints are:

$$\begin{aligned} Q_{reg}\Delta_{tmax} &\leq 1 \\ \Delta_{tmin} &\leq \Delta_{tmax} \\ 0 \leq Q_0 &\leq 2 \end{aligned} \tag{5.2}$$

Using this conditions, let $N : \mathbb{R}^6 \Rightarrow \mathbb{R}^4$ be defined as

$$N(Q_0, Q_{reg}, \tau_{inc}, \tau_{con}, \Delta_{tmin}, \Delta_{tmax}) := \begin{pmatrix} Q_{reg}\Delta_{tmax} - 1 \\ \Delta_{tmin} - \Delta_{tmax} \\ Q_0 - 2 \\ -Q_0 \end{pmatrix}. \tag{5.3}$$

Let $(Q_0, Q_{reg}, \tau_{inc}, \tau_{con}, \Delta_{tmin}, \Delta_{tmax})$ be a set of parameters, that fulfill the condition

$$N(Q_0, Q_{reg}, \tau_{inc}, \tau_{con}, \Delta_{tmin}, \Delta_{tmax}) \leq 0.$$

These parameters describe again an AV-level and the corresponding trajectory Q, which only uses values within the range $[0, 2]$. Hence, let $\Omega$ be the set of all in this meaning valid combinations of parameters, defined as

$$\Omega := \left\{ \omega = \begin{pmatrix} Q_0 \\ Q_{reg} \\ \tau_{inc} \\ \tau_{con} \\ \Delta_{tmin} \\ \Delta_{tmax} \end{pmatrix} : N(\omega) \leq 0, \omega_{min} \leq \omega \leq \omega_{max} \right\}, \tag{5.4}$$

where $\omega_{min}, \omega_{max} \in \mathbb{R}^6$ describe the parameter ranges.

## 5.2 MINLP formulation

Having updated the set of all possible parameters $\Omega$, also the model constraints must be reformulated. It is necessary to ensure a valid distance between every propagation as well as a valid value of $Q$ at every successful and silent impulse.

### Feasible Distance

The distance describes the relation between the pattern $m$, the propagation time-points $t_i$, their corresponding $\Delta_{t_i}$ and the two parameters $\Delta_{tmin}$ and $\Delta_{tmax}$. Certain conditions must be satisfied to ensure, that the model does not overstep the demanded range of variation regarding the distance between two beats.

The $\Delta_{t_i}$ are simply constrained by $\Delta_{tmin}$ and $\Delta_{tmax}$:

$$\Delta_{tmin} \leq \Delta_{t_i} \leq \Delta_{tmax} \qquad \forall i = 1, \ldots, n_{ECG} \tag{5.5}$$

Since the distances $\Delta_{t_i}$ are not constant anymore, every $t_i$ occurs in a certain interval in spite of known $m$ and $\omega$. These intervals depend on the time of the previous propagation and the minimal respective maximal distances $\Delta_{tmin}$ and $\Delta_{tmax}$. With $t_0 = 0$ this means:

$$\begin{aligned} t_1 - t_0 &\leq (m_1 - 1)(\Delta_{t,1} + (m_1 - 2)\Delta_{tmax}) \\ t_i - t_{i-1} &\leq \Delta_{t_i} + (m_i - 1)\Delta_{tmax} && \forall i = 2 \dots n_{ECG} \end{aligned} \tag{5.6}$$

and

$$\begin{aligned} t_1 - t_0 &\geq (m_1 - 1)(\Delta_{t,1} + (m_1 - 2)\Delta_{tmin}) \\ t_i - t_{i-1} &\geq \Delta_{t_i} + (m_i - 1)\Delta_{tmin} && \forall i = 2 \dots n_{ECG} \end{aligned} \tag{5.7}$$

The distance between two beats minus the known $\Delta_{t_i}$ is less or equal to the maximal distance $\Delta_{tmax}$ times every previous silent beat and greater or equal to the minimal distance $\Delta_{tmin}$ times every previous silent beat. Since the first impulse occurs at $t_0 = 0$, $m_1$ must be decreased by 2 instead of 1. Also, this condition only active if $m_1 > 1$, otherwise it would hold $t_1 = t_0 = 0$. Therefore, the factor $(m_1 - 1)$ deactivates the constraint in that case.

If the $t_i$ observe the constraints (5.6) and (5.7), they all occur in valid intervals and do not violate the condition of the maximal respective minimal beat distance.

Using (5.5), (5.6) and (5.7), two new constraints can be formulated to ensure that every beat occur only in its valid interval. Let $H_1 : \mathbb{Z}^{n_{ECG}} \times \mathbb{R}^{n_{ECG}} \times \mathbb{R}^{n_{ECG}} \times \mathbb{R}^{n_\omega} \to \mathbb{R}^{2n_{ECG}}$ be defined as

$$H_1(m, t, \Delta, \omega) = \begin{pmatrix} \Delta_{t,1} - \Delta_{tmax} \\ \Delta_{tmin} - \Delta_{t,1} \\ \vdots \\ \Delta_{t,n_{ECG}} - \Delta_{tmax} \\ \Delta_{tmin} - \Delta_{t,n_{ECG}} \end{pmatrix} \leq 0$$

Let then $H_2 : \mathbb{Z}^{n_{ECG}} \times \mathbb{R}^{n_{ECG}} \times \mathbb{R}^{n_{ECG}} \times \mathbb{R}^{n_\omega} \to \mathbb{R}^{2n_{ECG}}$ be defined as

$$H_2(m, t, \Delta, \omega) = \begin{pmatrix} t_1 - t_0 - (m_1 - 1)(\Delta_{t,1} + (m_1 - 2)\Delta_{tmax}) \\ t_0 - t_1 + (m_1 - 1)(\Delta_{t,1} + (m_1 - 2)\Delta_{tmin}) \\ t_2 - t_1 - \Delta_{t,2} + (m_2 - 1)\Delta_{tmax} \\ t_1 - t_2 + \Delta_{t,2} + (m_2 - 1)\Delta_{tmin} \\ \vdots \\ t_{n_{ECG}} - t_{n_{ECG}-1} - \Delta_{t,n_{ECG}} + (m_{n_{ECG}} - 1)\Delta_{tmax} \\ t_{n_{ECG}-1} - t_{n_{ECG}} + \Delta_{t,n_{ECG}} + (m_{n_{ECG}} - 1)\Delta_{tmin} \end{pmatrix} \leq 0$$

The time points $t_i$ and the corresponding $\Delta_{t_i}$ cannot overstep their feasible range while satisfying these conditions.

### Constraints for propagated beats

As in the previous approach, the value of $Q$ must be below $Q_{max} = 1$ to propagate all necessary beats:

$$Q(t_i) \leq 1 \qquad \forall i = 1, \dots, n_{ECG}$$

The resulting constraint is very similar to the one needed by using a constant shift $\Delta_t$. In fact, due to the explicit appearance of $t$, the formulation is even simplified. Let $H_3 : \mathbb{Z}^{n_{ECG}} \times \mathbb{R}^{n_{ECG}} \times \mathbb{R}^{n_{ECG}} \times \mathbb{R}^{n_\omega} \to \mathbb{R}^{n_{ECG}}$ be the new constraint function with

$$H_3(m, t, \Delta, \omega) = \begin{pmatrix} Q_0 + 0 - t_1 \cdot Q_{reg} - 1 \\ Q_0 + 1 - t_2 \cdot Q_{reg} - 1 \\ \vdots \\ Q_0 + (n_{ECG} - 1) - t_{n_{ECG}} \cdot Q_{reg} - 1 \end{pmatrix} \leq 0$$

If $H_3$ is satisfied, every beat $t_1, \dots, t_{n_{ECG}}$ is successful. All constraints $H1$, $H2$ and $H3$ can now be combined to one condition in the form of a weak inequality. Let $H : \mathbb{Z}^{n_{ECG}} \times \mathbb{R}^{n_{ECG}} \times \mathbb{R}^{n_{ECG}} \times \mathbb{R}^{n_\omega} \to \mathbb{R}^{5n_{ECG}}$ be therefore defined as

$$H(m, t, \Delta, \omega) = \begin{pmatrix} H_1(m, t, \Delta, \omega) \\ H_2(m, t, \Delta, \omega) \\ H_3(m, t, \Delta, \omega) \end{pmatrix} \leq 0.$$

**Constraints for silent beats**

The value of $Q$ must be above $Q_{max} = 1$ at every silent beat:

$$Q_0 + (i - 1) - (t_i - \Delta_{t_i})Q_{reg} > 1 \qquad \forall i \in I,$$

where $I$ is the index set containing every $i$, whose $t_i$ have a previous silent impulse:

$$I := \{i : i \in [1, \dots, n_{ECG}], m_i \geq 2\} = \{i_1, \dots, i_{|I|}\}.$$

Again, there are only slightly changes in this constraint compared to the equivalent one using a constant $\Delta_t$. Let $J_I : \mathbb{Z}^{n_{ECG}} \times \mathbb{R}^{n_{ECG}} \times \mathbb{R}^{n_{ECG}} \times \mathbb{R}^{n_\omega} \to \mathbb{R}^{|I|}$ be defined as

$$J_I(m, t, \Delta, \omega) = \begin{pmatrix} Q_0 + (i_1 - 1) - (t_{i_1} - \Delta_{t_{i_1}})Q_{reg} - 1 \\ Q_0 + (i_2 - 1) - (t_{i_2} - \Delta_{t_{i_2}})Q_{reg} - 1 \\ \vdots \\ Q_0 + (i_{|I|} - 1) - (t_{i_{|I|}} - \Delta_{t_{i_{|I|}}})Q_{reg} - 1 \end{pmatrix} > 0.$$

Satisfying this constraint, every impulse between the desired beats is now silent.

**Combining the Results**

The defined constraints ensure all necessary properties to formulate a similar characterization as in lemma 4.1 of an AV-Level, described by the Q-Model.

**Lemma 5.1.** *Let* $(m, t, \Delta, \omega) \in \mathbb{Z}^{n_{ECG}} \times \mathbb{R}^{n_{ECG}} \times \mathbb{R}^{n_{ECG}} \times \Omega$ *be chosen such that* $H(m, t, \Delta, \omega) \leq 0$ *and* $J_I(m, t, \Delta, \omega) > 0$*. Then* $m$ *is a feasible generated pattern for the AV-level, specified by* $\omega$*,* $t$ *and* $\Delta$*, to simulate* $n_{ECG}$ *propagations.*

*Proof.* Since the uniqueness of $m$ is not guaranteed while using non-fixed time-shifts $\Delta_{t,j}$, it must only be shown that the combination $(m, t, \Delta, \omega)$ is in fact a valid characterization of an actual simulation.

To do this, one must only reconsider the previous results. First, the constraint $H$ ensures that the $t_i$ do not extend their feasible intervals, specified by $\omega$, $\Delta$ and $m$. If this is true, $H$ further ensures that the value of $Q$ is below or equal to 1 at every demanded propagation $t_1, \ldots, t_{n_{ECG}}$. On the other hand, $J$ prevents the value of $Q$ to also be suitable for a propagation at the foregone failed impulses. Therefore, all necessary properties of $Q$ within this time-horizon are only fulfilled if neither of those conditions is violated. $\square$

Using this lemma, one can again check whether a combination ($m$, $t$, $\Delta$, $\omega$) results in the desired amount of output beats without an explicit simulation. Also, if such a valid combination is known, the complete trajectory $Q$ is again evaluable over the complete time horizon of the simulation.

### Formulating the Objective

Since the calculation of the propagation delay has not changed, also the objective need only be slightly adapted. Reconsidering the formulation of the objective in chapter 4.3, the delay has the form

$$r_i = t_i + \tau_{con} + \tau_{inc} Q(t_i) \qquad \forall i = 1, \ldots, n_{ECG}.$$

The $t_i$ are explicitly known and the value of $Q$ is therefore easy to determine. Let $S : \mathbb{Z}^{n_{ECG}} \times \mathbb{R}^{n_{ECG}} \times \mathbb{R}^{n_{ECG}} \times \mathbb{R}^{n_\omega} \rightarrow \mathbb{R}^{n_{ECG}}$ be defined as

$$\begin{aligned} S(m, t, \Delta, \omega) &= \begin{pmatrix} t_1 + \tau_{con} + \tau_{inc} Q(t_1) \\ t_2 + \tau_{con} + \tau_{inc} Q(t_2) \\ \vdots \\ t_{n_{ECG}} + \tau_{con} + \tau_{inc} Q(t_{n_{ECG}}) \end{pmatrix} \\ &= \begin{pmatrix} t_1 + \tau_{con} + \tau_{inc}(Q_0 + 0 - t_1 Q_{reg}) \\ t_2 + \tau_{con} + \tau_{inc}(Q_0 + 1 - t_2 Q_{reg}) \\ \vdots \\ t_{n_{ECG}} + \tau_{con} + \tau_{inc}(Q_0 + (n_{ECG} - 1) - t_{n_{ECG}} Q_{reg}) \end{pmatrix} \end{aligned}$$

### Formulating the MINLP

The problem can now be formulated as a mixed-integer nonlinear problem with a least squares objective function.

$$\begin{aligned} \min_{m,t,\Delta,\omega} \quad & \|S(m, t, \Delta, \omega), ECG\|_2 \\ \text{s.t.} \quad & H(m, t, \Delta, \omega) \leq 0 \\ & J_I(m, t, \Delta, \omega) > 0 \\ & m \in \mathbb{Z}^{n_{ECG}} \\ & t, \Delta \in \mathbb{R}^{n_{ECG}} \\ & \omega \in \Omega \end{aligned} \tag{5.8}$$

# 6 Numerical Results

The previous theoretical results showed that both Mobitz- and Wenckebach-type AV-blocks can be emulated by the Q-model using suitable parameters. Single Mobitz- and Wenckebach-type AV-blocks can therefore only explain a real subset of possible simulation results of the Q-Model. Assuming a measured sequence of R-R intervals, the Q-model can therefore always emulate this pattern with an equal or even smaller error than an emulation only with static Mobitz- or and Wenckebach-type blocks. However, Scholz et al. build their AV-blocks out of multiple singular elements. This is also an extension of such static simulations. Hence, the exact relation between MAVBA and the Q-Model cannot be stated trivially.

It is the overall ambition to improve the informative value of the generated simulations. In this case, this means an increase of the sensitivity and specificity when discriminating atrial flutter and atrial fibrillation. Since a small error value indicates atrial flutter, the quality of the discrimination only rises if the improvement of the objective value, primarily affects these cases. A sample solving algorithm to solve MINLP (4.13) was implemented to get first numerical results. In the long term, the achieved performance will determine whether the Q-model is suitable to discriminate between atrial flutter and atrial fibrillation.

The Q-model was tested on two sets of real ECG data[5] [2]. Both datasets represent cases of atrial flutter and consist of 20 ventricular contractions. The implementation in this thesis is limited to the MINLP (4.13).

## 6.1 First Algorithmic Approach

In chapter 4.3 were defined two types of constraints for the MINLP using regular impulses:

1. Weak inequalities to describe the parameter set $\Omega$ and the constraint $H$.

2. Strict inequalities $J_I$ depending on a set $I$ of active indices.

The first type can easily be formulated to match common solver requirements. On the other hand, there are a few difficulties to directly apply the constraints $J_I$ without further modifications.

In general, the following is demanded:

$$J_I(m, \omega) > 0,$$

with

$$I := \{i : i \in [1, \ldots, n_{ECG}], m_i \geq 2\} = \{i_1, \ldots, i_{|I|}\}.$$

Using this constraint in common solvers requires formulations.

### Relaxation As A Weak Inequality

Processing strict inequalities poses various computational difficulties. It is therefore desirable to replace this condition by a more practical one. The constraint can be approximated by using

[5] The study design was approved by the ethics committee of the University of Heidelberg and conforms to the standards defined in the Helsinki Declaration.

the relaxation

$$
\begin{aligned}
& J_I(m,\omega) \geq \vec{\epsilon} \\
\Leftrightarrow \qquad & J_I(m,\omega) - \vec{\epsilon} \geq 0,
\end{aligned}
$$

for $\vec{\epsilon} = (\epsilon, \dots, \epsilon)^T \in \mathbb{R}^{|I|}$ and a suitable small $\epsilon > 0$. Due to the non-exact arithmetic of computer-based solvers, a tolerance $\epsilon$ near the machine-accuracy will only have a negligible influence on the result quality. With this approximation, the explicit handling of the strict inequality is avoided.

### Dissolving The Index Set $I$

The constraint $J_I$ should only be applied to those indices contained in $I$. Therefore, the constraint corresponding to $i \notin I$ is inactive if $m_i = 1$. To ensure this behavior for all constraints, the decisive term $(m_i - 1)$ can simply be added as a factor to disable unused conditions. Let $J : \mathbb{Z}^{n_{ECG}} \times \mathbb{R}^{n_\omega} \to \mathbb{R}^{n_{ECG}}$ describe this new requirement as

$$
\begin{aligned}
J(m,\omega) &:= \begin{pmatrix} (m_1-1)(Q(t_1-\Delta_t) - Q_{max} - \epsilon) \\ (m_2-1)(Q(t_2-\Delta_t) - Q_{max} - \epsilon) \\ \vdots \\ (m_{n_{ECG}}-1)(Q(t_{n_{ECG}}-\Delta_t) - Q_{max} - \epsilon) \end{pmatrix} \\
&= \begin{pmatrix} (m_1-1)(Q_0 - 1 - (M_1-2)\,\Delta_t Q_{reg} - \epsilon) \\ (m_2-1)(Q_0 - (M_2-2)\,\Delta_t Q_{reg} - \epsilon) \\ \vdots \\ (m_{n_{ECG}}-1)(Q_0 + (n_{ECG}-2) - (M_{n_{ECG}}-2)\,\Delta_t Q_{reg} - \epsilon) \end{pmatrix} \\
&\geq 0.
\end{aligned}
$$

Reconsidering the definition of $J_I$, this constraint ensures that the value of $Q$ is above $Q_{max} = 1$ at every silent beat that occurs directly before each propagation $t_i$. If $m_i = 1$, meaning there is no silent beat between the two successful propagations $t_{i-1}$ and $t_i$, the factor $(m_i - 1)$ now disables this constraint in $J$ by fixing it to 0.

This approach does not further affect the possible accuracy.

However, in this thesis a slightly different condition is implemented to compute the numerical results. The used alternative has the advantage reduced constraint complexity.

Let $\bar{J} : \mathbb{Z}^{n_{ECG}} \times \mathbb{R}^{n_\omega} \to \mathbb{R}^{n_{ECG}}$ be defined as

$$
\begin{aligned}
\bar{J}(m,\omega) &:= \begin{pmatrix} Q_0 - 1 - (M_1-2)\,\Delta_t Q_{reg} - \epsilon \\ Q_0 - (M_2-2)\,\Delta_t Q_{reg} - \epsilon \\ \vdots \\ Q_0 + (n_{ECG}-2) - (M_{n_{ECG}}-2)\,\Delta_t Q_{reg} - \epsilon \end{pmatrix} \\
&\geq 0.
\end{aligned}
$$

In this case, the inequalities must be fulfilled regardless of whether such a silent beat actually exists. Fortunately, this only has a minor bearing on cases without such silent impulses. To see this, let $t_{i-1}$ and $t_i$ be two consecutive beat. Then it holds for the value of $Q$:

$$\begin{aligned} Q(t_{i-1}) &\in [0,1] \\ Q(t_i) &\in [0,1] \end{aligned}$$

Since there is now silent impulse between $t_{i-1}$ and $t_i$, it follows

$$\begin{aligned} t_i &= t_{i-1} + \Delta_t \\ \Rightarrow Q(t_i) &= Q(t_{i-1}) + 1 - \Delta_t Q_{reg} \end{aligned}$$

The condition described by $\bar{J}$ constrains the value of $Q(t_i - \Delta_t)$. This value of $Q$ at $t_i$ can be determined depending only on $t_{i-1}$, as

$$\begin{aligned} Q(t_i - \Delta_t) &= Q(t_i) + \Delta_t Q_{reg} \\ &= Q(t_{i-1}) + 1 - \Delta_t Q_{reg} + \Delta_t Q_{reg} \\ &= Q(t_{i-1}) + 1. \end{aligned}$$

$\bar{J}$ now demands:

$$\begin{aligned} & Q(t_i - \Delta_t) - 1 - \epsilon \geq 0 \\ \Leftrightarrow \quad & Q(t_{i-1})\epsilon \geq 0 \end{aligned}$$

Therefore, using $\bar{J}$ instead of $J$ restricts the value range of $Q(t_{i-1})$ to

$$Q(t_{i-1}) \in [\epsilon, 1].$$

This limitation only slightly reduces the interval, in which $Q(t_{i-1})$ could possibly occur. Therefore, the effect on the simulation quality is also negligible in the following test cases.

### Parameter Ranges

Since Scholz et al. have obtained good results with MAVBA, the value range of the Q-model parameters is based on their used bounds. In table (2) the used parameters are compared to the one used by MAVBA. While the time shift $\Delta_t$ and the cardiac circle length CL can directly be adapted, a few adjustments are necessary to apply to the remaining variables.

The constant propagation delay $\tau_{con}$ respective $\mathrm{AV_M/AV_W}$ is fixed to 50 ms. In the formulation of the Q-model the parameter $\tau_{con}$ also describes the offset of the first impulse in the

| Parameter | LB | UB | Parameter (MAVBA) | LB (MAVBA) | UB (MAVBA) |
|---|---|---|---|---|---|
| $\Delta_t$ | 198 ms | 350 ms | CL | 198 ms | 350 ms |
| $Q_0$ | 0 | 2 | - | - | - |
| $Q_{reg}$ | 0.001 | $\frac{1}{198}$ | - | - | - |
| $\tau_{con}$ | -300 ms | 50 ms | $\mathrm{AV_M/AV_W}$ | 50 ms | 50 ms |
| $\tau_{inc}$ | 60 ms | 300 ms | $\Delta$ | 20 ms | 100 ms |
| $m_i$ | 1 | 5 | - | - | - |

LB = Lower Bound, UB = Upper Bound

Table 2: Parameter ranges

simulation as described earlier in chapter 4.2. The first beat of the used test data always occurs at $t_0$. With a fixed constant shift of 50 ms and the maximal linear shift of 300 ms, the first actual impulse could enter the AV-node up to 350 ms before this first beat. The variable $\tau_{con}$ must express this offset by allowing a negative time shift of up to 350 ms below the constant shift of 50 ms, which results in the used -300 ms.

The linear delay $\tau_{inc}$ depends in the value of $Q$. This value is always within the interval $[0, 1]$ if an impulse is propagated. The dynamic delay can therefore vary within the range $[0, 300]$. The parameter $\Delta$, used by MAVBA, is a constant delay that is added after every successful propagation in a Wenckebach-type AV-block. In order to emulate a similar behavior, the maximal delay of the Q-model must accommodate the maximal delay generated by a delay of multiple times $\Delta$.

The regeneration rate $Q_{reg}$ must observe the limit that would allow to restore more than one whole beat within $\Delta_t$. Hence, the overall upper bound for this parameter is $\frac{1}{198}$, depending on the smallest time shift $\Delta_t$. The lower bound allows a minimum regeneration to skip up to 4 impulses. The remaining $Q_0$ must simply observe the general range of the trajectory $Q$.

The integer parameters $m_i$ must be at least 1. The upper bound is set to 4, allowing at most 4 failed impulses between two beats.

### Experimental Implementation

Performing these reformulations, all constraints have the commonly used form of a weak inequality. These suitable constraints were used to implement a first solving routine in Matlab. The core of this sample algorithm is the solver BONMIN[6] as delivered within the OPTI Toolbox[7].

The solver needs a feasible initial value for all optimization variables $(m, \omega) \in \mathbb{Z}^{n_{ECG}} \times \mathbb{R}^{n_\omega}$. This can be done by using the simple pattern of alternating successful and failed propagations:

$$m := (2, 2, \dots, 2)^T$$
$$\omega := (Q_0, Q_{reg}, \tau_{inc}, \tau_{con}, \Delta_t)^T = (1.5, 0.002, 0, 100, 250)^T$$

Reconsidering the problem formulation of the MINLP (4.13), the objective is the least-squares error between the simulated and the measured R-R intervals on the surface ECG:

$$\min_{m,\omega} \quad \|ECG - S(m, w)\|_2$$

The objective can directly be implemented. This provides the last item to solve the problem with BONMIN.

### Dataset 1: Patient 21

Appendix (A.1) describes the dataset of patient 21. MAVBA was able to find an optimal emulation with a scaled least-squares error of 0.0660. The simulation used a predicted cardiac cycle length of 285 ms and a single level Wenckebach-type AV-block. The Q-Model, by contrast, fails to achieve the desired result. Even with a feasible initial value, the solving-algorithm was only able to find a feasible solution for a simulation horizon of eight beats. Figure 5 and table 5 illustrate the found solution.

[6] Basic Open-source Nonlinear Mixed INteger programming, http://www.coin-or.org/Bonmin/

[7] http://www.i2c2.aut.ac.nz/Wiki/OPTI/index.php

### Dataset 2: Patient 49

The dataset of patient 49, described in appendix (A.2), could be solved with a scaled error-value of 0.0415 by MAVBA. The algorithm was able to determine a regular cardiac cycle length of 278 ms, using a single-level Wenckebach-block. The BONMIN-based solver could end with a feasible result simulating up to nine beats. The optimal solution stated in table (4) and figure 6 shows a very close approximation to the used 278 ms by MAVBA. Moreover, both simulated patterns match within the time horizon.

## 6.2 Discussion

At this early stage, it is impossible to make accurate predictions regarding the potential of the Q-model. To this end, further effort must be invested into finding a more stable solving algorithm in order to obtain a significant amount of test results.

What can be noted, however, is that the single-level formulation seems to be unsuitable to sufficiently describe the first dataset. While the Q-model performs well on smaller time horizons for this example, a larger amount of beats cannot be emulated by a single block level. The approach of building a single AV-block out of multiple elements has a clear advantage in this scenario. A multi-level approach could provide the necessary generality to also successfully emulate this case.

However, given the promising first numerical results of the second dataset and the theoretical basis it is highly likely that the Q-model can perform well on certain cases. What is more, it is also likely that these properties could be transferred to future multi-level approaches by using the same Q-model definition as examined in this thesis.

On balance, it is a matter of debate whether the simulations of this more general approach can successfully support the discrimination of atrial flutter and atrial fibrillation; or whether the Q-model performs only well on an unspecific set of problems, including both cardiac arrhythmias.

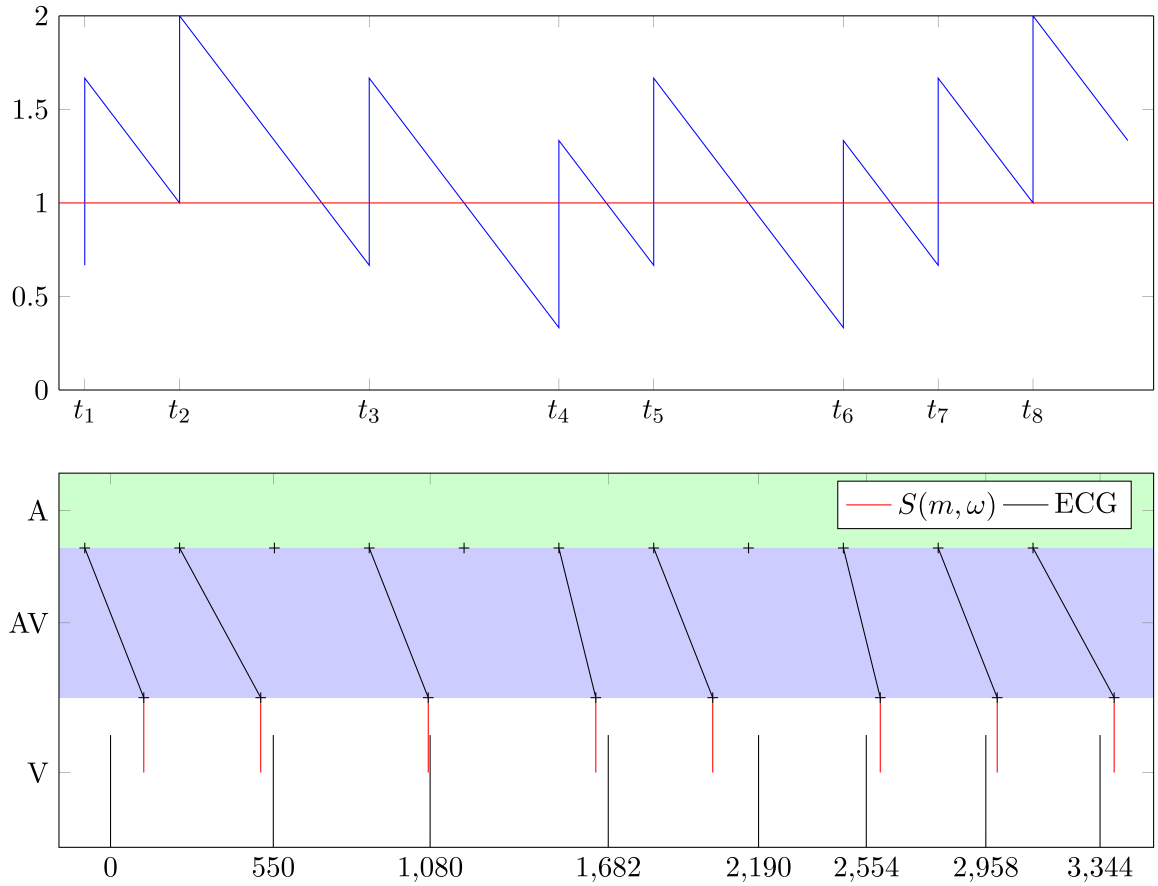



Figure 5: Best Found Emulation for Patient 21. A = Atria, AV = AV-node, V = Ventricles, LSQ = 46218.4762

| Parameter | Value | Parameter | Value | Result | Value |
|---|---|---|---|---|---|
| $Q_0$ | 0.6667 | $m_1$ | 1 | $r_1$ | 112.3333 |
| $Q_{reg}$ | 0.0021 | $m_2$ | 1 | $r_2$ | 507.5238 |
| $\tau_{inc}$ | 224.1905 | $m_3$ | 2 | $r_3$ | 1073.7142 |
| $\tau_{con}$ | -37.1270 | $m_4$ | 2 | $r_4$ | 1639.9047 |
| $\Delta_t$ | 320.4603 | $m_5$ | 1 | $r_5$ | 2035.0952 |
| | | $m_6$ | 2 | $r_6$ | 2601.2857 |
| | | $m_7$ | 1 | $r_7$ | 2996.4761 |
| | | $m_8$ | 1 | $r_8$ | 3391.6667 |

Table 3: Optimal Solution for Patient 21

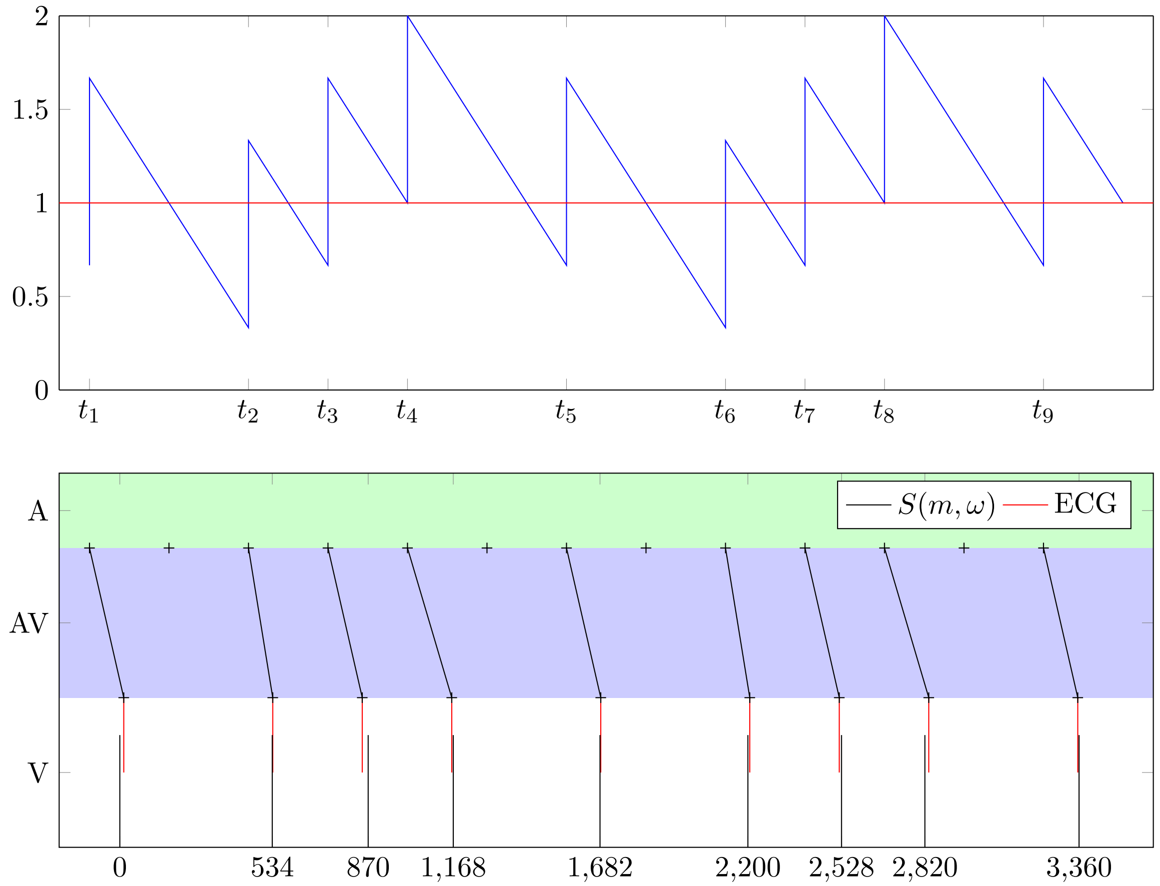



Figure 6: Best Found Emulation for Patient 49. A = Atria, AV = AV-node, V = Ventricles, LSQ = 970.4285

| Parameter | Value | Parameter | Value | Result | Value |
|---|---|---|---|---|---|
| $Q_0$ | 0.6667 | $m_1$ | 1 | $r_1$ | 13.8095 |
| $Q_{reg}$ | 0.0024 | $m_2$ | 2 | $r_2$ | 535.7381 |
| $\tau_{inc}$ | 105.0714 | $m_3$ | 1 | $r_3$ | 849.2381 |
| $\tau_{con}$ | -56.2381 | $m_4$ | 1 | $r_4$ | 1162.7381 |
| $\Delta_t$ | 278.4762 | $m_5$ | 2 | $r_5$ | 1684.6667 |
| | | $m_6$ | 2 | $r_6$ | 2206.5952 |
| | | $m_7$ | 1 | $r_7$ | 2520.0952 |
| | | $m_8$ | 1 | $r_8$ | 2833.5952 |
| | | $m_9$ | 2 | $r_9$ | 3355.5238 |

Table 4: Optimal Solution for Patient 49

# 7 Recapitulation

Using the idea of a degree of exhaustion to describe the behavior of single AV-levels within multilevel AV-blocks, this thesis gives a first introduction in the Q-model as an unified approach to describe Mobitz- and Wenckebach-type blocks. Starting with an easy comprehensible draft, all redundant parameters were excluded. This led to a unique formulation and an understanding of the model behavior. With this knowledge, an easy to use lemma could be stated to characterize the feasibility of the parameters determining the models trajectory. The resulting MINLP formulation is suitable for finding the best set of parameters to emulate measured R-R intervals. This solving process completely avoids the use of any explicit simulation of the AV-level and is able to handle continuous variables. The model was further expanded to allow variations within the input signal.

In addition to these results, further effort is needed to determine whether this new approach can enhance the accuracy of discriminating between atrial flutter and atrial fibrillation or is unsuitable make reliable predictions.

### Prospects

An important key-step to make actual statements about the accuracy of the Q-model is to further analyze the problem of the formulated MINLP. This will help to better understand the resulting problem dynamics and structure, for example the convexity of the constraints and the objective function. This should then allow the finding or development of a suitable solving-algorithm. This is necessary to evaluate the validity of the Q-model as an emulation for second-degree AV-blocks. This evaluation will hopefully show that this new approach is a convenient alternative to serve the mentioned problem of Scholz et al. of finding a more generalized and continuous formulation.

Moreover, an important point is a model-extension to also emulate complex multilevel blocks. Besides understanding the resulting model dynamics, it is crucial to find a suitable problem approach. This formulation should still allow the use of continuous parameters. A major challenge is the fixation of the number of parameters and therefore the problem dimension. Using only single-level blocks, this was possible by implicitly handling the silent impulses with the vector $m$. This was only possible due to the already known number of necessary propagations.

Using multiple AV-blocks, this fixation only applies to the last level. In such a model, the result of the first level would serve as the input for the second one. A chance in the vector $m$ of the second block therefore changes the amount of necessary beats in the first block. Hence, the formulation approach used so far cannot directly be adapted to also fit multi-level problem structures.

A further understanding of consecutive AV-blocks could help finding a smart formulation that exploits the problem structure and can handle these varying dimensions implicitly. The analysis of single level AV-blocks with a non-constant time shift $\Delta_{t,j}$ therefore hopefully is a first step towards future extensions.

## References


[1] Statistisches Bundesamt. Häufigste Hauptdiagnosen in deutschen Krankenhäusern nach Geschlecht im Jahr 2013 (in 1.000). http://de.statista.com/statistik/daten/studie/218758/umfrage/haeufigste-hauptdiagnosen-in-deutschen-krankenhaeusern-nach-geschlecht/, 2013. [Online; accessed 29-April-2014].

[2] Eberhard P. Scholz, Florian Kehrle, Stephan Vossel, Alexander Hess, Edgar Zitron, Hugo A. Katus, and Sebastian Sager. Discriminating atrial flutter from atrial fibrillation using a multilevel model of atrioventricular conduction. *Heart Rhythm*, 11(5):877 – 884, 2014.

[3] *Clinical Cardiac Electrophysiology Techniques and Interpretations*. Lippincott Williams & Wilkins, 3th edition, 2001.

[4] Wikipedia. Woldemar Mobitz — Wikipedia, The Free Encyclopedia. http://de.wikipedia.org/wiki/Woldemar_Mobitz, 2013. [Online; accessed 29-April-2014].

[5] Wikipedia. Karel Frederik Wenckebach — Wikipedia, The Free Encyclopedia. http://de.wikipedia.org/wiki/Karel_Frederik_Wenckebach, 2014. [Online; accessed 29-April-2014].

[6] Rice University. Cardiac muscle and electrical activity. http://cnx.org/contents/14fb4ad7-39a1-4eee-ab6e-3ef2482e3e22\@7.16:127/Anatomy_&_Physiology, 2014. [Online; accessed 29-April-2014].

[7] Sebastian Sager. Personal communication, 2014.

[8] Wikipedia. AV-Block — Wikipedia, The Free Encyclopedia. http://de.wikipedia.org/wiki/AV-Block, 2015. [Online; accessed 29-April-2014].

# A Appendix

## A.1 Dataset Patient 21

| Beat | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|
| Time [ms] | 0 | 550 | 1080 | 1682 | 2190 | 2554 | 2958 | 3344 | 3790 | 4190 |
| Beat | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 |
| Time [ms] | 4802 | 5316 | 5936 | 6504 | 7068 | 7632 | 8202 | 8748 | 9334 | 9904 |

Table 5: ECG Pattern Patient 21 [2]

## A.2 Dataset Patient 49

| Beat | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|
| Time [ms] | 0 | 534 | 870 | 1168 | 1682 | 2200 | 2528 | 2820 | 3360 | 3882 |
| Beat | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 |
| Time [ms] | 4436 | 4782 | 5296 | 5812 | 6152 | 6674 | 7194 | 7528 | 7886 | 8322 |

Table 6: ECG Pattern Patient 49 [2]

## A.3 MAVBA Result Patient 21

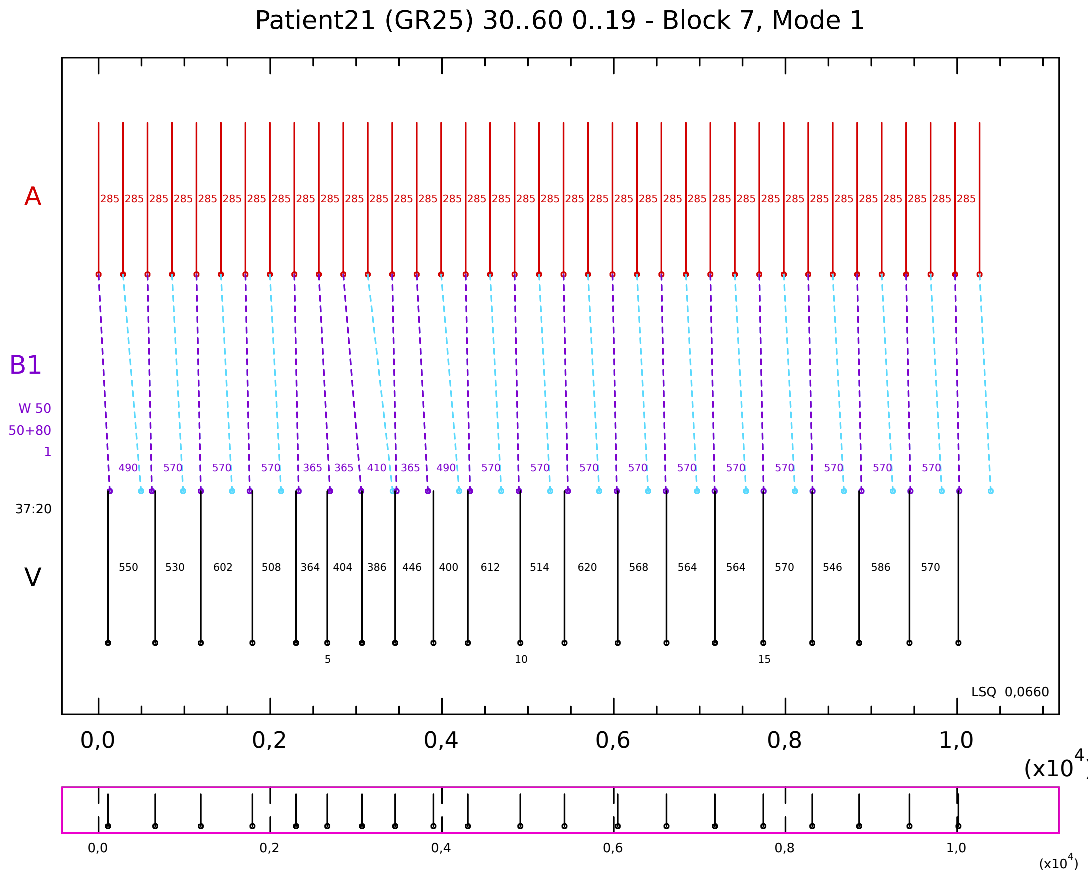



Figure 7: MAVBA Result Patient 21 [2]

## A.4 MAVBA Result Patient 49

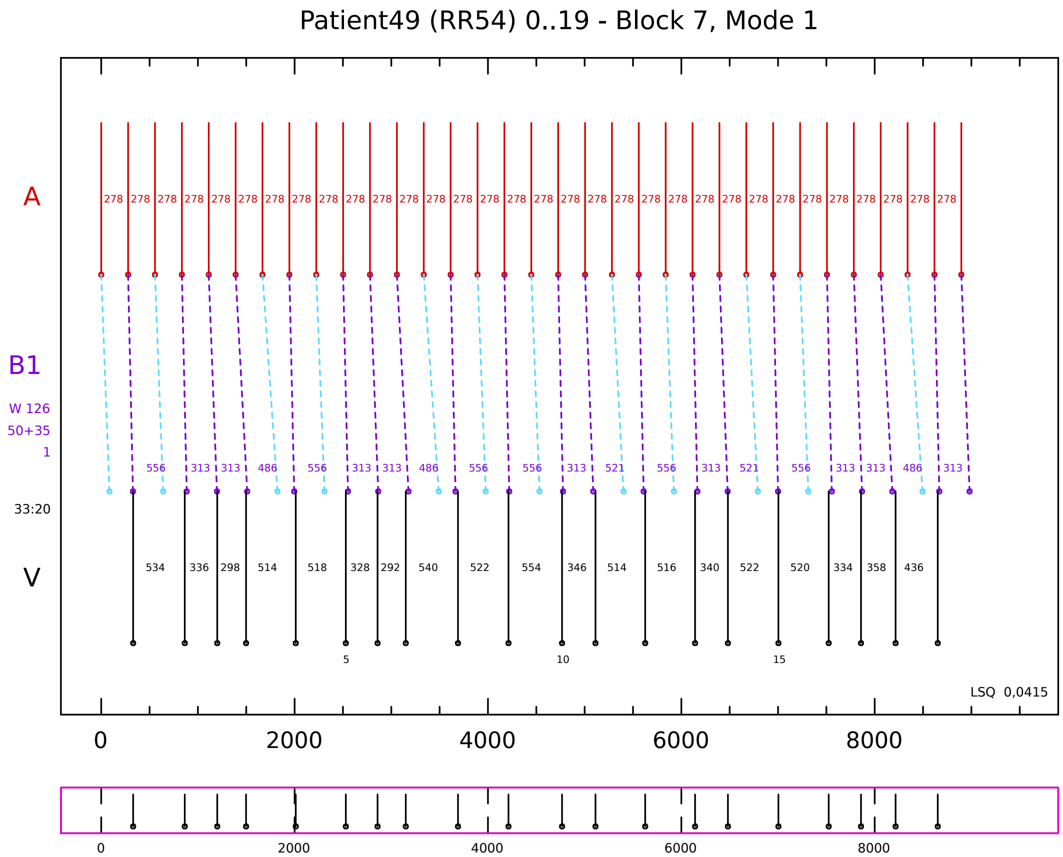



Figure 8: MAVBA Result Patient 49 [2]

## Erklärung

Hiermit erkläre ich, dass ich die vorliegende Arbeit selbstständig und ohne Benutzung anderer als der angegebenen Quellen und Hilfsmittel angefertigt habe.

Magdeburg, 30. April 2015