A Mathematical Model To Study Reentrant Cardiac Arrhythmias

Proefschrift

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To my parents

To Doortje
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"The great tragedy of Science -
the slaying of a beautiful hypothesis by an ugly fact"

T.H. Huxley
(1825-1895)
Collected Essays
Chapter 1.

Introduction

1.1 Historical overview

In 1561, the noble Rutgerus of Randwick, mayor of Gennep, Holland, visited his physician Johann Weyer because of palpitations. Dr Weyer described the pulse of Rutgerus of Randwick as having an intermittent rhythm with every third beat a so-called ‘pulsus caprizans’. (1) Although at that time the interpretation of the pulse and the accompanying prognosis, as described by Galen (2) in the second century were still considered to be valid, Weyer recognised already, that the outcome of a disease not only depended on the characteristics of the pulse but also on the underlying condition of the patient.

Also for this patient, Weyer was right. Rutgerus did not die from his arrhythmia, but recovered after a copious evacuation. He was slain in 1583, murdered by a group of Spanish riders. (3)

Galen’s interpretation of the pulse and its prognostic significance remained valid until the 17th century. But Galen was not the first author interested in the arterial pulsations and their abnormalities.

Already in 500 BC. the art of feeling the pulse was known in China. Approximately in the year 280, a classic treatise on the pulse published in ten volumes was available in China. Roughly at the same time the “Pen tsao” (= System of Medicine) was published. In the sixth century it took Li Shi 30 years to compile it for publication. Using this method location and site of all diseases could be derived by studying the accompanying pulse. (4 - 5)

At the end of the 19th century it was possible to record the mechanical pulse, and to register the electrical activity using the capillary electrometer. (6)

It was not until the beginning of the 20th century, that cardiac rhythm could be studied in a more easy and accurate way.

In 1906 Einthoven, professor in Physiology and Chancellor of the University of Leiden, presented at the occasion of the 331st anniversary of the University his ideas about the use and the advantages of registration of the electrical activation of the heart with the help of the string galvanometer. Using this device he was able to make registrations of good quality. Referring to the fact that the patient in the hospital, and the cardiograph in his laboratory were connected over a long distance by telephone wires (1) the first registrations were named “Telecardiograms”. At the same time Einthoven made some interesting remarks about the value of electrophysiological research and its relation to medicine. (7) He stated:

... physiology is no longer only pleasant entertainment, like the reading of a simple novel for a serious reader of scientific literature, but indeed an important and
necessary subject of study...

The introduction of the recording of the electrical activity of the heart by a string galvanometer, was an important step on the long way to clinical electrophysiology of today.

In 1906 Einthoven showed that by using different electrode positions potentials of different morphology could be recorded. He also gave examples of 2:1 atrioventricular block, extrasystoles, bigeminal rhythm and dextrocardia. In the same article he suggested the study of the influence of the administration of drugs on atrioventricular conduction. (8)

Although the electrical registration of human cardiac activity was introduced in the beginning of this century, several decades passed before a more direct approach to the study of rhythm and conduction disturbances in the intact human heart became possible.

Important landmarks in the study of arrhythmias were the introduction of the recording of intra-cardiac potentials by Latour en Puech in 1957 (9) and the combination of intracardiac recordings coupled with programmed stimulation of the human heart by Durrer (10) in 1967. In that study the authors demonstrated in four patients with the WPW syndrome the initiation and termination of circus movement tachycardia by using properly timed electrical stimuli.

This was followed shortly thereafter by the development of a reliable catheter technique to record the His bundle electrogram in the human heart. (11)

The availability of these intracardiac stimulation and recording techniques accelerated the accumulation of knowledge on conduction and rhythm abnormalities in man.

In 1971 Wellens (12) described the use of programmed stimulation of the heart in patients with atrial flutter, AV nodal tachycardia and the pre-excitation syndromes. One year later he reported on the use of this technique in patients suffering from ventricular tachycardia. (13)

In patients suffering from tachycardia clinical electrophysiological studies can be of great help in determining the underlying mechanism of the arrhythmia and the selection of treatment. (14)

These investigations however, are not without risks, relatively unpleasant to the patient, expensive, and time and personnel consuming (15) The study and understanding of mechanisms of tachycardias in patients using electrophysiological investigations is difficult because only limited data are available:

- Most patients are investigated only a few times.
- The number of healthy volunteers to study impulse formation and conduction in the normal heart is almost nil.
- Many electrophysiological parameters are influenced by the autonomic nervous system. These changes are difficult to quantify and to control and cannot be reproduced at will. (16)
Because of these limitations and also because of ethical reasons, it is impossible to perform certain studies in the intact human heart, like the effect of chronic drug intoxication on impulse formation and conduction. In such cases the use of an animal model can be of great help. Using such a model it is possible to repeat an experiment several times under well defined laboratory conditions. The fluctuations in sympathetic and vagal tone and their influences on electrophysiological parameters, are however very difficult to control in the intact animal model and extrapolation to the human heart is difficult.

To simulate electrophysiological experiments in a reproducible way, without spontaneous or autonomic fluctuations in any parameter, one can use a mathematical model. This requires that the investigator describes all different parts of the model and defines the relations between them. Following a mathematical description, the investigator can use actual values obtained during an electrophysiological study to test the effect(s) of various perturbations on the model. In such a model both the consequences of changes in parameters as selected by the investigator, and the effect of the introduction of extrastimuli can be studied.

By defining basic electrophysiological properties of the model and the induced changes, the investigator will be able to test hypotheses that originate during clinical electrophysiological investigations in man. Also multiple changes and combinations of changes in electrophysiological properties, which can not be investigated during the clinical simulation study, can now be studied under defined circumstances. While attractive, computer simulation also has its limitations as will be shown later.

The use of a mathematical model to study electrophysiological properties of the heart is not new. Several models have been used to study aspects of cardiac electrophysiology, such as:

a) Basic cardiac electrophysiology (17 - 26)
b) Reconstruction of the electrocardiogram (27 - 41)
c) Simulation of the function of some parts of the conduction system of the heart (42 - 45)
d) The simulation of the total heart or parts of it, to study mechanisms, observed during clinical electrophysiological studies. (46 - 50)

a) Basic cardiac electrophysiology

Mathematical models have been developed to study the generation of impulses and their conduction to adjacent cells. Some of these models describe quantitatively membrane potentials, propagation of action-potentials and interference between two individual pacemakers. (17-23). Sharp for instance (20), combined numerical methods for solving cable equations and previously published models for membrane properties to simulate cardiac impulse propagation along a unidimensional strand. Decreased excitability and changes in intercellular
coupling could be simulated. All these models were based on data from the cellular level derived from experiments using microelectrode techniques. The contribution by Hodgkin and Huxley (24) on mechanisms of impulse generation and propagation through a core-conductor model of propagation can be considered a standard work, forming the basis for several other models. In their work they introduced a model of an excitable cell on which the so-called Hodgkin-Huxley equations are based.

Recently van Capelle (25) published a study about impulse propagation in a two-dimensional model. In this model sheets consisting of coupled excitable elements were used to simulate arrhythmias. Before simulation starts the geometry of the network, the amount of coupling between elements and the electrophysiological properties of the elements, describing excitability, automaticity, and refractory period are defined. After defining the contour of the sheet of elements, using a joystick and a graphic display of the contour, elements can be removed, leaving holes in the sheet. In the same way connections between elements can be deleted, changed or added and the type of cells of the different elements can be modified. Using the same technique, the site of stimulation and the elements selected to be monitored on the terminal are determined. The activation of each element is recorded on a disk file for further interpretation. Using a sheet of these elements it was possible to simulate both focal and reentrant arrhythmias. The author suggests that the spatial interaction could play an important role in this type of investigations.

It is of interest that many investigators describing impulse propagation concentrated upon intestinal tissue beside cardiac tissue because of its less complicated morphology as compared to the cardiac tissues. (26)

All models so far discussed describe the heart in its basic state or allow the summation of a small number of elements.

b) Reconstruction of the electrocardiogram.

One of the oldest models to reconstruct the cardiogram was developed by Van der Pol in 1928. (27)

In 1965 Silvester showed in an analog model, that it was possible to simulate the vectorcardiogram. (28) To do so he divided the heart in 20 segments, each containing an independent time varying dipole. This model of a 20 dipole heart was located in an inhomogeneous volume conductor to simulate the torso. This was followed a few years later by a digital version. (29 - 30) Using these more powerful techniques the resolution was increased considerably. The Purkinje fiber distribution having homogeneous conduction velocity and the sites of first activation determined during animal experiments have to be given to the model. Myocardial lesions of 7-10 mm diameter and 2-3 mm thickness can be recognised in the simulated cardiograms.

In the model designed by Min in 1974, a matrix of relaxation oscillators coupled in two directions was used to describe the electrical activity in smooth muscle like stomach and small intestine. To describe these oscillators a group of non-linear differential equations were applied. This made it possible to simulate the normal
electrocardiogram, some arrhythmias and the use of an external pacemaker. (31) Also in the model of Rosenberg one is able to simulate a number of arrhythmias. (32)

In many of these models designed to reconstruct the surface electrocardiogram, special attention is given to the influence of size and shape of the thorax on the configuration of the electrocardiogram. (33 - 41).

In 1978 Miller presented a digital model for the simulation of body surface electrocardiograms during the ventricular activation and recovery (33) Using approximately 4000 elements in a three dimensional array, a reconstruction of the ventricles of the heart was made. These 4000 elements were grouped into 23 regions. Data about the excitation sequence and the action potentials were taken from the literature. By summing up all potentials in each region the dipole representing that region can be calculated. By combining these 23 dipoles and assuming the heart to be surrounded by a homogeneous volume conductor with the shape of an adult male torso, the potentials on the surface could be simulated.

In the same issue of Circulation Research Miller described the simulation of ischemia and infarction. (34) This was based on the hypothesis that ischemia is reflected by a decrease in the magnitude of the resting potential and changes in action potential duration. By progressively modifying the action potentials in those elements representing the area of ischemia, the electrocardiographic signs of ischemia could be simulated.

Anterior and inferior transmural ischemia and infarction and anterior subendocardial ischemia could be simulated.

Based on the assumption that the ventricles (apart from the septum) have an eccentric spherical configuration, Hori (35) developed a mathematical model of the activation of the ventricles. Like others he divided the ventricle in a number of small elements each containing one dipole. To calculate the behaviour of every dipole data derived during animal experiments were used. In this model a few limitations are present. 1) There is no intraventricular septum. 2) The eccentric spherical model does not duplicate the morphology of the ventricles satisfactory. 3) The conduction velocity in the conduction system and the myocardium is assumed to be constant.

In the model constructed by Ritsma van Eck (37) a much more accurate representation of the morphology of the two ventricles was given.

In this 3-dimensional model the ventricle was reconstructed using 155000 regularly packed rhombodecahedra, each with a volume of 1.28 mm³. The endocardial surface was covered by a network of Purkinje cells. Each myocardial cell was assumed to be at rest, activated or refractory. The time delay between the activation of adjacent cells represents the conduction velocity. Also in this model laboratory data were used to determine the first sites and times of activation.

In the study of Rudy and Plonsey (38) special emphasis was given to the influence of variations in the location of the heart on the potentials measured at the epicardium. The effect of the surface layer and subcutaneous fat on these potentials was shown to be minimal. In a second study the author (40) used this model of eccentric spheres to determine the influence of a number of factors on the electrocardiogram. They studied the influence of the blood pool on these potentials,
anemia and polycythemia. Low lung conductivity (emphysema), low and high
pericardial and myocardial conductivity was simulated and the influence on the
electrocardiogram was studied. The influence of low skeletal muscle conductivity,
obesity, a thick myocardium protruding into the lung region, increase of myocardial
wall at the expense of the blood cavity and finally the position of the heart in the
torso was determined.
Ranney (41) simulated the surface electrocardiogram using potentials directly
measured on the epicardial surface instead of using a number of dipoles. To do
so 90 electrodes were chronically implanted on the ventricle. Heart to body
surface transfer coefficients were derived from the measured geometric
coordinates of all the electrodes, assuming a homogeneous volume conductor
between the epicardium and the body surface.
In the study by Arntzenius et al. (36) several different models designed to
reconstruct the heart are discussed.

c) Simulation of the function of some parts of the conduction system of the heart

These models are developed to describe and investigate the function of parts of
the cardiac conduction system.
In 1971 Omena made an analog model of the conduction in cardiac tissue, using a
tunnel diode. (42)
This was followed in 1973 by a mathematical description of conduction through
the AV Node by Heethaar. (43) To analyse AV nodal conduction an isolated
perfused rat heart was stimulated using a variety of impulse sequences such as
fixed rates and frequency steps. The response was measured on the left ventricular
epicardium. Using these data a mathematical description of the AV node was
determined. By stimulating the atrium at a random cycle length, which was longer
than the AV nodal refractory period, the ventricular response was determined
and compared with the mathematical model. It was shown to be possible to
determine the atrial cycle length or the AV nodal conduction time from the
ventricular cycle length. After including the influence of refractoriness in the
behaviour of the model the influence of blocked impulses can be studied.
It appears that the influence of a blocked impulse and a conducted impulse on
the conduction time can be calculated using the same mathematical equations. In
this model Wenckebach conduction can be demonstrated. The same author also
constructed an analog model of AV nodal conduction to find a physiological
explanation for the mathematical relationships found during AV nodal conduction
(44-45). A transmission line of coupled excitable cells was used obeying the
Bonhoeffer-Van der Pol equations. The reaction of the transmission line on fixed
rates of stimulation and frequency steps was compared with the behaviour of the
AV node in animal experiments.

d) Simulation of the total heart or parts of it, to study mechanisms observed
during clinical electrophysiological studies

Only in this group of mathematical models mechanisms of arrythmias and
relevance of clinical observations can be studied.
In these models the conduction system or parts of it have been simulated. This
allows testing of hypotheses from clinical electrophysiological investigations.
To simulate the whole heart one cannot use a model based on a description of impulse propagation between cells. Such a model would be enormous because millions of coupled oscillators have to be taken into consideration. Furthermore during clinical electrophysiological investigations the properties of these cells are not known.

In 1982 Holley used a 3-dimensional model of the ventricles to simulate ventricular tachycardia. (46)

Our group has previously reported on the use of a mathematical model to study factors influencing stability of a circus movement tachycardia. (47-48) During an invasive electrophysiological investigation in a patient a characteristic pattern of termination of a circus movement tachycardia was observed. Using data on AV nodal conduction, a single purpose model to study this alternation of the tachycardia cycle length prior to termination, was constructed. The findings using this model were compared with the clinical data. Both were in complete agreement. These results were used to verify the behaviour of the model described in this thesis. Using a mathematical model, we also described that some of the criteria advanced as diagnostic for triggered activity as mechanism of a tachycardia, can also be observed in arrhythmias using a reentry circuit. (49)

A major problem with investigations using mathematical models is the need to design a completely new model for every simulation study because new components of circuits involved in conduction of impulses have to be used. It is of interest that all these mathematical models have some parts in common.

To make simulation studies available to a larger field of users, a general model of electrical conduction through the heart was designed. The specifications and properties of such a model are described in this thesis. The limitations of such a general simulation model will be discussed also.

1.2 The philosophy behind the model

The aim of this study was to develop a mathematical model to facilitate research in clinical electrophysiology. We therefore wanted to have a model whose structure and components would allow implementation of data derived from clinical studies.

Invasive electrophysiological investigations can be performed for different reasons.

1) To localize the site of the abnormality in the conduction system in patients with conduction disturbances.
2) To study the mechanisms of tachycardias.
3) To select the best medication to protect the patient against the recurrence of arrhythmias.
4) To increase our knowledge of the 12 lead electrocardiogram by correlating findings from electrophysiological investigations with the surface electrocardiogram.

In our department clinical electrophysiological investigations are performed as follows.
After local anaesthesia, the femoral vein is punctured and catheters are introduced percutaneously and positioned in the heart under fluoroscopic control. The following locations of the catheter are most often used: 1) the high right atrium, 2) across the tricuspid valve ring to record His bundle electrograms, 3) the coronary sinus to record and stimulate the left atrium, 4) the apex of the right ventricle. To record and stimulate the left ventricular apex, the catheter is introduced retrogradely to the left ventricle using the femoral artery or using a transseptal approach in patients with a patent foramen ovale. Catheters are used for recording the local activity and to deliver electrical stimuli. By using uni- or quadrupolar catheters stimulation and registration from one site can be performed simultaneously.

By recording activation times from the different catheters conduction times between the different sites of the heart can be determined. These measurements of conduction times are performed during sinus rhythm and during pacing at different cycle lengths. The relation between heart rate and conduction time can be studied. Using a basic paced rhythm and one extra stimulus, the refractory period of the different parts of the conduction system of the heart can be determined. By using different sites and different stimulation cycle lengths initiation and termination of tachycardias is studied and the influence of medication on arrhythmias evaluated. During the investigation all signals are recorded simultaneously and continuously on 16 channel paper and stored on tape. The paper speed used (100 mm/s) gives a measurement accuracy of 5 to 10 ms.

During these electrophysiological investigations information of the electrophysiological properties of the heart at the cellular level does not become available. Also knowledge about the exact topographical and morphological aspects of the conduction system in the patient under study cannot be obtained. This makes it impossible to reproduce the activation of the heart in a way as done in the Kitsema van Eyk model.

Furthermore information about the electrophysiological properties of the intact human heart is limited, because the number of sites of observation using intracardial catheters has to be restricted for practical reasons. As described, by using catheter techniques one can obtain information about conduction between different sites of the heart. It gives values on conduction velocity and the duration of refractory period of tissue between the sites of the different catheter tips.

In general to be useful our model should fulfill the following criteria:

- It should resemble reality as closely as possible, especially in relation to stimulation studies performed in the intact human heart.
- It should be based on a modular concept. This will enable flexibility both in the layout of the conduction pathways, as in the electrophysiological properties of these pathways.
- The behaviour of the model should be logical and understandable.
- Results should be presented in a uniform way, at an acceptable computing speed.

The model described in this thesis has to fulfill the following extra requirements:

- Only data should be used that can be derived from invasive electrophysiological investigations. Not in the first place to be able to reproduce the activation in each patient who undergoes electrophysiological investigation, but to be able to test hypothesis derived from finding during these studies.

- The model should be applicable without special knowledge about handling computers. The program has to collect all input data in a ergometric way. This input of data and the resulting output of results should be performed using a syntax understandable for clinical electrophysiological investigators.

By constructing the model in this way, not using coupled oscillators (which properties cannot be determined during invasive electrophysiologic investigation) all these conditions can be fulfilled.

Approaching the study of reentry arrhythmias using network analysis techniques makes it possible to translate clinical hypotheses directly into computer language.

In the development of this mathematical model a number of assumptions have been made of which some cannot be tested and other apparently are made arbitrarily. For example the assumed homogeneity of different segments, the absolute refractoriness of an element, (an element is refractory or excitable, there is no state inbetween), the selection of a simulation cycle length of 1 ms and the subdivision of a segment in 100 elements. In this thesis a rationale will be given at the time of making these assumptions.

In the model only tachyarrhythmias on the basis of reentry will be simulated. Other mechanisms of arrhythmias like parasystole can be simulated in the model, but only as an independent source of impulse formation.
Chapter 2.

Description of the mathematical model used to simulate clinical cardiac electrophysiology

2.1 The model
2.2 Simulation studies
2.3 The 33 different segment states
2.4 Order of handling
2.5 Handling of a segment without changes in electrophysiological parameters or new impulses
2.6 The introduction of a new impulse
2.7 Consequences of short refractory periods and non constant conduction velocity

2.1 The model

As mentioned in chapter 1 the structure of the mathematical model is based upon observations obtained during invasive clinical electrophysiological studies in man.

During these investigations catheters are introduced into the heart at a number of sites. At these sites the intracardiac electrical activity is recorded and programmed electrical stimulation performed to study conduction between different parts of the heart and the mechanisms of tachycardias.

With the information obtained by these techniques, one can design a network, built of segments, in which the segments represent the pathways between different sites in the heart. In this network we assume that the impulse is able to propagate along the different segments in only anterograde, retrograde, or both directions. Segment properties depend on the electrophysiological data, measured with help of the catheters. The junctions between the different segments in our model represent the catheter positions used in the patients.

This approach allows the implementation of observations from electrophysiological studies into a mathematical network.

By using information about the electrophysiological properties of the segments in between two junction points as obtained during programmed stimulation of the heart values from clinical electrophysiological studies can be put into the model.
Fig 2.1.1. gives an example from a patient with the Wolff-Parkinson-White syndrome having a left sided accessory pathway between the atrium and the ventricle.

![Diagram of heart with labeled points](image)

**FIGURE 2.1.1.**

Legend to figure 2.1.1.

This figure is a schematic drawing of the heart and its conduction system. As shown, there are six junction points, representing the catheter positions (open circles) used during the electrophysiological investigation. The segments are located between the junction points, indicating that conduction between these points in at least one direction is possible. Catheter positions: 1. High Right Atrium; 2. Low Right Atrium; 3. Coronary Sinus; 4. His Bundle region; 5. Right Ventricle; 6. Left Ventricle. Note that on the left side of the heart an accessory pathway is present enabling conduction between atrium and ventricle over this structure.

**Definitions**

Conduction time in one segment: the time required for an impulse to travel through a segment from one junction point to the next one. These times can be related to the cycle length of the last cycle (so-called rate-dependency).

The refractory period of a segment is the longest time interval between two successive impulses during which the second impulse is unable to penetrate into a segment in the same direction.

In the model described hereafter a segment can either be excitable or refractory. No intermediate possibility exists in this model.

In clinical electrophysiology it is very difficult to differentiate between the partially refractory and the complete refractory state. Since the model is only using data that can be derived during these clinical studies, the relative refractory phase has been ignored and only two states are accepted: refractory or excitable.

The segments of the model have homogeneous electrophysiological properties which do not change during the conduction of an impulse through the segment. This does not mean that each impulse through the segment has the same conduction...
time or that the segment has always the same refractory period. Both can be changed for example in relation to the rate of impulses going through the model. During conduction through a segment, however, the conduction velocity is considered to be constant.

Although it is rather unlikely that all electrophysiological parameters are distributed homogeneously over a segment, there is no better information available. The properties of a segment, derived during electrophysiologic investigations are also determined over the whole segment independent of the actual distribution of these properties.

The conduction velocity and the refractory period are defined in anterograde as well as in retrograde direction. This is done because electrophysiologic properties of parts of the cardiac conduction system can be, and frequently are, different in anterograde and retrograde direction.

Unidirectional block in a segment is represented in our model by inability to conduct in one direction. If unidirectional block would have been represented by extremely slow conduction through a segment, permanent block occurs in the direction opposite to conduction.

An impulse travelling through a segment is followed by a refractory sector. The length of this refractory sector is determined by the time of activation of the first element, the conduction velocity in the segment and the duration of the refractory period. The first activated element is the first one to be excitable again after termination of the refractory period. After a certain period of time following activation of an element, not all elements within a segment will be refractory. The elements activated first can again be excitable. The elements which at a certain time interval are still inexcitable are considered to form a tail of refractoriness.

As soon as the first element becomes excitable again the refractory or excitable state of the segment is defined by the position of the tail. In the same direction, impulse and tail travel with the same velocity.

To define the position of the impulse and the tail, each segment is divided into 100 elements. Element 1 is the first element used, when an anterograde impulse is conducted through the segment. During retrograde conduction element 100 is the first one activated. When an anterograde impulse has reached or passed the element 100, the impulse is considered to have left the segment, leaving behind a certain number of refractory elements.

The subdivision of a segment in 100 elements is arbitrary. By increasing the number of elements the accuracy will only increase if the simulation cycle length decreases with the same magnitude. This procedure will increase computing time. More information on the relation between computing time and resolution is given in paragraph 4.2.

Another important concept of the model is the collision point. If an anterogradely and a retrogradely conducted impulse collide, the collision point within the segment is calculated. This calculation is made by taking into account the old positions of the impulses together with the conduction velocities in both directions.

Usually at both sides of the collision point a part of the segment is refractory. The
collision point is always the last activated element of a segment, and the last one to become excitable again.

Conduction velocities are defined as the number of elements in a segment (100), divided by the conduction times in ms. Conduction velocity is defined both in anterograde (AV) and retrograde (RV) direction.

Conduction distances in each direction are defined as the number of elements passed by an impulse during one simulation cycle, (see below) in each direction. They are also defined anterogradely (AD) and retrogradely (RD).

In the model simulation cycle lengths of 1 ms have been selected arbitrarily. Longer cycle lengths to increase simulation speed, or shorter cycle lengths to increase temporal resolution are possible however. The best resolution achieved using registrations on paper is 8 till 10 ms. Using a simulation cycle length of 1 ms the model is always more accurate than these registrations.

**Segment states.**

Every segment is defined by its state and the value of its parameters. In figure 2.1.2, a schematic representation of a segment is presented. An impulse is penetrated in the anterograde direction.

![FIGURE 2.1.2.](image)

Legend to figure 2.1.2.
The figure shows a segment with an anterogradely partially conducted impulse. The position of the impulse (AP) is indicated by an open circle. The refractory part of the segment is marked by the shaded area. The number one in this figure indicates the first (excitable) element. The time this element will remain refractory represents the refractory state of the segment after a conducted impulse.

AP indicates the position of the impulse in the segment. If the impulse is located at position no 1, it means that the impulse has just entered the segment. If the impulse reaches position 100, or passes it, the impulse is considered to have left the segment and the value of AP returns to zero. An AP value of zero indicates therefore that no impulse is being conducted through the segment.

![FIGURE 2.1.3.](image)

Legend to figure 2.1.3.
This figure shows a segment with an anterogradely vanishing tail. The position of the refractory tail is indicated by an open square. The symbols used in figure 2.1.2 and 2.1.3 will be used in following illustrations. In these illustrations a collision point (CP) will be indicated by a black circle, the position of a retrogradely conducted impulse by RP, and the retrograde vanishing tail by RL.
As soon as the time for refractoriness at the first excitable element has returned to zero, some elements will become excitable again during the next simulation cycle. The Al (Anterograde tail) represents the end of the refractory tail after conduction of an impulse. It is processed in the same way as an impulse is processed.

2.2 Simulation studies

A simulation study contains the following five parts.

1) Defining the network.
   The site and number of junction points are selected. The segments representing pathways, are located between these junction points.

2) Defining the electrophysiological properties of the segment. The properties of the segments are defined, including: conduction velocity, refractory period and ability of an impulse to be conducted into one or both directions.

3) Defining the initial state. If at the start of the simulation study the network is not conducting impulses and no segment is (partially) refractory, all segments are in state 1. (see paragraph 2.3).

4) The actual computation.
   During the simulation process a certain sequence of operations is continuously repeated.
   a) The first operation is the calculation of the state of each segment after one more cycle. To calculate the new state, the present state and electrophysiological properties of the segment are considered. The different possibilities are described in detail in paragraph 2.5.
   b) In the second step the introduction of an impulse into a segment is considered. This impulse can be conducted from one segment to a junction point and from there into all the segments that are connected to that junction point. The impulse can also be entered over a free end of a segment, that means a junction point connected to one single segment. Before an impulse can enter a segment a number of conditions have to be fulfilled. In paragraph 2.6 these conditions are listed.
   c) In the third step the model tests whether or not the electrophysiological properties of one or more of the elements have changed. The possible consequences of a change in electrophysiological parameters are listed in paragraph 2.7.

5) Presenting the results.
   Results can be presented in three different ways:
   a) The time of activation of a junction point is given, together with the number of the segment which was conducting this impulse. Also when applicable the occurrence of a collision point is reported. This enables the user to draw ladder diagrams of activation through the conduction system.
b) After every computational cycle (or a multiple of cycles) all parameters of one or more segments can be printed. This makes is possible to study very accurately the behaviour of a part of the conduction system. The amount of data, however, is too big to use this method over a long period of time.

c) In special circumstances it is possible to represent the defined network on a high-resolution graphic display. The position of impulses, tails and collision points can be displayed realistically. The amount of work required however, limits this application only to didactical purposes.

2.3 The 35 different segment states

Considering the definitions and limitations as described in detail in paragraph 2.7., only 35 different states of a segment are required to define the possible states of a segment. These states (ST) will be described in more detail below. By limiting the number of states to 35, the structure of the model remains simple and computer time can be reduced.

1. The segment is not electrically activated, there is no impulse within the segment and all elements of the segment are excitable. The segment is able to conduct the next impulse.

2. There is one impulse being conducted anterogradely. This leaves all the elements up to the last conduction refractory. Ahead of the impulse all the elements of the segment are excitable.

3. All elements of the segment are refractory as the result of a previous anterogradely conducted impulse. The state of the whole segment is defined by the time period the first activated element on the left side will remain refractory.

4. The last activated element on the right side of the segment are still refractory. The part on the left side of the segment which was activated earlier is potentially able to conduct a new impulse. The length of the refractory part of the segment is defined by the position of the tail in the segment.

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ST 5. This is a combination of the second and the fourth state. A part of the segment is still refractory, caused by a previously anterogradely conducted impulse. A, the excitable left side of the segment an impulse has entered the segment. The impulse is conducted anterogradely at a fixed distance behind the tail, since the conduction velocity of the impulse and the tail are considered to be equal.

ST 6. This state is essentially identical to the second situation. However, the impulse is now being conducted retrogradely through the segment.

ST 7. As in state three, all elements of the segment are refractory. In contrast to the third state, this is the result of a previously retrogradely conducted impulse.

ST 8. The left side of the segment is still refractory because of a previously retrogradely conducted impulse. The right side of the segment is no longer refractory and is potentially able to conduct an impulse retrogradely.

ST 9. A retrogradely conducted impulse follows a tail at a fixed distance, through the again excitable part of the segment on the right side.

ST 10. An impulse is conducted both in anterograde and retrograde direction. After a period of time these two impulses will collide and create a collision point, leaving the whole segment refractory on both sides of the collision point.
ST 11. As predicted in state 10 the anterograd and retrograde conducted impulses created a collision point, leaving the whole segment refractory. The refractory period on the left and the right side of the collision point may or may not be equal in length.

ST 12. The left part of the segment, made refractory by a previously anterogradely conducted impulse is able to conduct impulses again at the beginning of the segment. The elements on the right side of the collision point are still completely refractory.

ST 13. This is the reverse of state no. 12. Now starting at the right side of the segment, some elements are potentially excitable.

ST 14. The elements on the left side of the segment, up to the collision point, made refractory by a previously anterogradely conducted impulse, have recovered completely. The elements on the right side of the collision point are still refractory.

ST 15. The reverse of state 14. On the left side of the collision point all elements are still refractory. On the right side, however, all elements are again excitable.

ST 16. Both ends of the segment are again excitable, but on the right side of the collision point some elements are still refractory.
ST 17. Also in this situation both ends of the segment are again excitable. The reverse is shown from above.

ST 18. While both ends of the segment are excitable, some elements on the left and the right side of the collision point are still refractory.

ST 19. This situation represents the ultimate one, before the segment can be considered totally electrically excitable again. By definition it will last for only one stimulation cycle.

ST 20. Anterogradely an impulse is conducted in the direction of the collision point. Some elements on the right side of this impulse up to the collision point are still refractory. All elements on the right side of the collision point are still refractory, caused by a previously retrogradely conducted impulse.

ST 21. All elements on the left side of the collision point are still refractory. On the right side of the collision point, only some elements are still excitable. At the right end of the segment a new impulse is conducting through the segment in retrograde direction.

ST 22. On the left side of the collision point an impulse is conducted in anterograde direction. Between this impulse and the collision point all elements are excitable. On the right side of the collision point all elements are still refractory.
ST 23. On the left side of the segment all elements are refractory up to the collision point. On the right side of the collision point an impulse is conducted in retrograde direction. All elements between this impulse and the collision point are excitable.

ST 24. Anterogradely up to the collision point the segment is electrically excitable. Retrogradely there is a refractory tail in between the collision point and a retrogradely conducting impulse.

ST 25. A tail of refractoriness from a previous retrogradely conducted impulse is present on the right side, up to the collision point. Anterogradely an impulse is conducted starting on the left end of the segment.

ST 26. In anterograde direction an impulse follows a tail in the direction of the collision point. On the right side of the collision point all elements are electrically excitable.

ST 27. On the left side of the collision point a tail of refractoriness created by an anterogradely conducted impulse is present. The right side is electrically excitable, apart from an impulse conducted in retrograde direction.

ST 28. Both on the left and on the right side of the collision point some elements are refractory. On the left excitable end an impulse is conducted in the anterograde direction.
ST 29. This is the reverse of situation 28.

ST 30. In this situation, as in the two previous ones, a collision point is present with a refractory tail at both sides. At both excitable ends an impulse is conducted in the direction of the collision point. These impulses are followed by a refractory tail.

ST 31. The refractory tails on the left and the right side of the collision point have disappeared. An antegrade conducted new impulse followed by a refractory tail has entered the left side of the segment.

ST 32. The reverse of situation 31.

ST 33. The state of the collision point is the same as in situations 31 and 32. There is an collision point without refractory tail at both sides. From both the left and the right side of the segments, an impulse is conducted into the direction of the collision point.

ST 34. Also in this situation two impulses are conducted in antegrade and one in retrograde direction are occurring. In between there is a collision point with a retrograde refractory tail.

ST 35. This situation is the reverse of situation 34.
2.4 Order of handling.

Possibilities

First we will discuss the handling of impulses, which have been introduced into a segment in an earlier simulation cycle, the handling of the refractory tail and the collision point.

In paragraph 2.6 the introduction of external impulses will be discussed and lastly in paragraph 2.7 the influence of changes in electrophysiological parameters.

The 35 different states are all constructed using three different parameters, an impulse, (i) a tail (t) and a collision point (c). To select a uniform order of handling all combinations were considered and one selected (i, t, c).

Considering three different parameters (i, t, c), six different permutations are possible:

\[
\begin{align*}
\text{i} & \quad \text{i} & \quad \text{t} & \quad \text{t} & \quad \text{c} & \quad \text{c} \\
\text{t} & \quad \text{c} & \quad \text{i} & \quad \text{c} & \quad \text{i} & \quad \text{t} \\
\text{c} & \quad \text{t} & \quad \text{c} & \quad \text{i} & \quad \text{i} & \quad \text{t}
\end{align*}
\]

The major decision to make is whether to handle in the final computer program an impulse before or after handling a tail.

If one selects the following sequence of handling: \(i \rightarrow t \rightarrow c\) (impulse, tail, collision point), it implies that looking in one direction, the minimum distance between the impulse and the end of the tail is greater than the distance over which an impulse can be conducted in one simulation cycle. Otherwise the impulse, being conducted first, will hit the tail running in front of it, which has not yet been handled.

When we select the sequence \(t \rightarrow i \rightarrow c\) (tail, impulse) this minimum distance is not required because the new position of the tail is determined first.

This minimum distance, which is chosen during the first order of handling, limits the number of possible new states, in this simulation program. An impulse which follows a tail cannot jump over that tail, or over a collision point in the same cycle. For example figure 2.4.1 shows a state of a segment and the possible states that can be reached during one simulation cycle.
FIGURE 2.4.1.

Legend to figure 2.4.1: This figure shows the states that can be reached in one simulation cycle starting from state 20. On the left side all states that can be reached handling the impulse first, are shown. On the right side all possible states using the order “Tail impulse” are indicated. Apart from the four states which are common to both cases 20, 22, 25, 28 there are two extra states possible: 11 and 13.

In these two situations an impulse conducts over the collision point in the same simulation cycle as the tail preceding the impulse. This increase in possibilities will increase the complexity and simulation time of the model.

The order of handling impulse-collision point has the consequence that the impulse first hits the collision point and then the model checks whether the collision point can be removed. This only makes a difference if an impulse hits a collision point with no tail at the opposite side. In the latter situation this will be removed in the same cycle.

For the order of handling tail-collision point the order obviously makes no difference.

The differences between these two options is marginal in normal cases. The maximum error in timing is one simulation cycle, which in most simulation studies equals 1 ms.

Following the above considerations the first option was selected, first to handle the impulse, then the tail and finally the collision point. By defining strictly the order of handling a reproducible and predictable handling of a segment can be performed.

Order of handling selected:

if any: Anterograde impulse
         Retrograde Impulse
         Anterograde Tail
         Retrograde Tail
         Collision Point
List of abbreviations used:

- AP: Anterograde Impulse \(1 \leq AP < 100\)
- RP: Retrograde Impulse \(1 < RP \leq 100\)
- AL: Anterograde Tail \(1 \leq AL < 100\)
- RL: Retrograde Tail \(1 < RL \leq 100\)
- CP: Collision Point \(1 < CP < 100\)
- AV: Anterograde conduction velocity
- RV: Retrograde conduction velocity
- AD: Anterogradely conducted distance (number of cells)
- RD: Retrogradely conducted distance (number of cells)
- AT: Anterogradely Refractory Timer. This indicates the time interval during which element 1 will remain refractory after an anterogradely conducted impulse.
- RT: Retrogradely Refractory Timer. This indicates the time interval during which element 100 will remain refractory after a retrogradely conducted impulse.
- PD: Proportional displacement. This variable is used to calculate the location of the collision point, taking into account the actual positions of the two colliding impulses and their conduction velocities. 
  \[ PD = \frac{RP - AP}{AD + RD} \]
- ARP: Anterograde Refractory Period. This parameter represents the anterograde refractory period of a segment. It can either be constant or rate dependent.
- RRP: Retrograde Refractory Period. Represents the retrograde refractory period.

2.5 Handling of a segment without changes in electrophysiological parameters or new impulses

In this paragraph the layout of the equations used to calculate the new state of a segment without introducing new impulses will be illustrated.

In all equations the subscript \(n\) or \(n+1\) represents the \(n^{th}\) or \((n+1)^{th}\) simulation cycle respectively.

To illustrate this layout the handling of two different states will be discussed in detail.
a) State 2 (ST 2)

In state 2 an impulse is being conducted anterogradely through a segment. In this state an impulse is conducted anterogradely (AP>0), there is no retrogradely conducting impulse (RP=0), there are no anterograde or retrograde tails, nor a collision point. (AL=0, RL=0, CP=0.) The element excited first is still refractory. (AT>0.) The retrograde refractory timer equals zero. (RT=0.)

\[ \text{AP}_n>0 \quad \text{RP}_n=0 \quad \text{AL}_n=0 \quad \text{RL}_n=0 \quad \text{AT}_n>0 \quad \text{RT}_n=0 \quad \text{CP}_n=0 \]

First the position of the anterograde impulse after one cycle is determined.

\[ \text{AP}_{n+1} = \text{AP}_n + AD \]

The new position of the impulse equals the old one plus the Anterograde Conduction Distance.

If the impulse reaches or passes the end of the segment (element 100) the variable representing the position of the impulse will be reset to zero (AP_{n+1}=0) and the new state of the segment will be indicated. (ST_{n+1}=ST 3).

If the impulse does not reach the end of the segment in this simulation cycle these values remain unchanged. (AP_{n+1}=AP_n+1 and ST_{n+1}=ST 2).

Summarized in computer terms:

\[
\begin{align*}
\text{IF} (\text{AP}_{n+1} \geq 100) & \quad \text{THEN} : \text{AP}_{n+1} = 0 & \quad \text{ELSE} : \text{AP}_{n+1} = \text{AP}_{n+1} \\
& \quad \text{ST}_{n+1} = \text{ST} 3 & \quad \text{ST}_{n+1} = \text{ST} 2
\end{align*}
\]

Finally the Anterograde Refractory Timer, indicating the time interval element 1 will remain refractory, is decreased by one.

\[ \text{AT}_{n+1} = \text{AT}_n - 1 \]

In the second example a more complicated state will be discussed.

b) State 20 (ST 20)

Again the description of the handling of this state starts with a description of the values of all parameters before the next simulation.

Anterogradely an impulse and a tail are present. (AP_n>0, AL_n>0) The first element is still refractory. (AT_n>0) Retrogradely there is no impulse and no tail present. (RP_n=0, RL_n=0). Element number 100 is still refractory. (RT_n>0). There is a collision point. (CP_n>0)

\[ \text{AP}_n>0 \quad \text{RP}_n=0 \quad \text{AL}_n=0 \quad \text{RL}_n=0 \quad \text{AT}_n>0 \quad \text{RT}_n>0 \quad \text{CP}_n>0 \]
After one simulation cycle there is still no retrograde impulse. \((RP_{n+1} = 0)\) The position of the collision point remains constant. \((CP_{n+1} > 0)\). The new position of the anterogradely conducted impulses equals the old one plus the Anterograde Conducted Distance. \((AP_{n+1} = AP_n + AD)\).

The new position of the anterograde conducted tail equals the old position plus the Anterograde Conduction Distance. \((AL_{n+1} = AL_n + AD)\).

\[
AP_{n+1} = AP_n + AD
AL_{n+1} = AL_n + AD
\]

At this moment the model should check, whether the end of the tail has reached the collision point. If yes this is indicated by resetting the variable describing the position of the anterograde tail \((AL_{n+1} = 0)\) and by defining the state to be equal to ST 22. If the tail does not reach the collision point these values are not changed.

\[
\text{IF } (AL_{n+1} = CP_n) \\
\quad \text{THEN : } AL_{n+1} = 0 \quad \text{ELSE : } AL_{n+1} = AL_n + 1 \\
\quad ST_{n+1} = ST 22 \quad ST_{n+1} = ST 20
\]

Thereafter both the Anterograde and the Retrograde Refractory Timers are decreased by one.

\[
AT_{n+1} = AT_n - 1 \\
RT_{n+1} = RT_n - 1
\]

After this decrement it is possible that element 100 is no longer refractory. In that case, if \(RT_{n+1} = 0\), the retrograde tail is given the value 100. Depending on the state of the segment two different states are possible. If the previous state represented ST 22, the new state will be ST 25. Otherwise the state will be ST 28. If this element is still refractory following this part of the simulation cycle both the values indicating the position of the retrograde tail and the state of the segment remain unchanged.

\[
\text{IF } (RT_{n+1} = 0) \\
\quad \text{THEN : } RL_{n+1} = 100 \quad \text{ELSE : } RL_{n+1} = 0
\]

\[
\text{IF } (ST_{n+1} = ST 22) \\
\quad \text{THEN } ST_{n+1} = 25 \quad \text{ELSE : } ST_{n+1} = ST 28
\]

In chapter 6 the handling of all 35 states has been listed.

### 2.6 The introduction of a new impulse.

The introduction of an impulse into a segment forms the second step in every simulation cycle. In the first step impulses which have been introduced into a segment during a previous simulation cycle have been handled together with possible tails and
collision points. In the second step the model tests, whether at any of the junction points impulses are considered to be conducted into those segments which are connected to that specific junction point.

This impulse can either be an impulse conducted through an adjacent segment or a new impulse from an internal or external impulse source.

Impulses can only be introduced into a segment from the junction points and not somewhere in a segment.

Because it is possible that during one simulation cycle at both ends an impulse waiting to be conducted into a segment is present, the following must be noted: the state of the segment changes as the result of an anterogradely or retrogradely introduced impulse. Therefore handling the second retrograde impulse requires the new state after handling the first impulse, and not the state of the segment as it was just before the handling of the first impulse.

Before an impulse can enter a segment the following condition must be fulfilled.

The conditions are given for an anterogradely conducted impulse. For a retrograde impulse the values can be derived easily.

The impulse can only penetrate a segment if at the beginning of that segment a number of elements equaling the Anterograde Conduction Distance (AD) does not contain a refractory tail conducting in the same direction. The presence of a collision point in this area, or an impulse in the opposite direction forms no objection against the introduction of an impulse. This free space prevents the impulse from jumping over a preceding tail in the next simulation cycle. If this condition is fulfilled, an impulse is introduced to position one and a timer (the Anterograde Refractory Timer) starts to count down the refractory period of the anterograde junction.

If this condition is not fulfilled, the potential impulse will be ignored.

To define the condition of a segment in cycle \( n + 1 \), based on the situation in cycle \( n \), a fixed procedure of handling is followed.

In the following part the introduction of an impulse in a segment depending on the state of that segment will be described in detail. Using three examples all different possibilities are shown.

Chapter 7 gives a complete description of the procedures used to handle new impulses for each of the 33 possible states.

In the formula used ARP and RRP represent the anterograde and retrograde refractory period respectively. They have been defined separately for each segment and can either be constant or rate dependent.

In the following examples \( n \) indicates the situation before, and \( n + 1 \) the situation after the introduction of an impulse into a segment.

Example 1. State 1.

As described in chapter 7 the introduction of a new impulse into a segment starts with a description of the present state.

In state 1, no elements are activated in the segment so all values are by definition equal to zero.
ST 1. \( A_{Pn} = 0, R_{Pn} = 0, A_{Ln} = 0, R_{Ln} = 0, A_{Tn} = 0, R_{Tn} = 0, C_{Pn} = 0 \)

All elements are excitable therefore an anterograde impulse can always be introduced into the segment.

The impulse will be introduced to position 1 \( (A_{Pn+1} = 1) \) and will set the Anterograde Refractory Timer equal to the Anterograde Refractory Period. \( (A_{Tn+1} = ARP) \). There is still no anterograde tail. \( (A_{Ln+1} = 0) \). In retrograde direction all values remain equal to zero. \( (R_{Pn+1} = 0, R_{Ln+1} = 0, R_{Tn+1} = 0) \). There is no collision point. \( (C_{Pn+1} = 0) \). After the introduction of an anterograde impulse the state of the segment changes into ST 2.

\[
\begin{align*}
A_{Pn+1} &= 1, \\
R_{Pn+1} &= 0, \\
A_{Ln+1} &= 0, \\
R_{Ln+1} &= 0, \\
A_{Tn+1} &= ARP, \\
R_{Tn+1} &= 0, \\
C_{Pn+1} &= 0, \\
S_{Tn+1} &= ST 2
\end{align*}
\]

Also in retrograde direction an impulse can always penetrate into such a segment. Now the impulse will be introduced to position 100 \( (R_{Pn+1} = 100) \) and the Retrograde Refractory Timer will be set equal to the retrograde Refractory Period. \( (R_{Tn+1} = RRP) \). There is no retrograde tail \( (R_{Ln+1} = 0) \). All anterograde values remain zero. \( (A_{Pn+1} = 0, A_{Ln+1} = 0, A_{Tn+1} = 0) \). There is no collision point. \( (C_{Pn+1} = 0) \). The new state of the segment is ST 6.

\[
\begin{align*}
A_{Pn+1} &= 0, \\
R_{Pn+1} &= 100, \\
A_{Ln+1} &= 0, \\
R_{Ln+1} &= 0, \\
A_{Tn+1} &= 0, \\
R_{Tn+1} &= RRP, \\
C_{Pn+1} &= 0, \\
S_{Tn+1} &= ST 6
\end{align*}
\]

In the second example the introduction of an impulse in a segment with one refractory end will be discussed.

State 2

The description starts again with a description of the present state.

ST 2. \( A_{Pn} > 0, R_{Pn} = 0, A_{Ln} = 0, R_{Ln} = 0, A_{Tn} > 0, R_{Tn} = 0, C_{Pn} = 0 \)

\( A_{Tn} > 0 \) indicates that the first element of the segment is still refractory. New impulses can not penetrate into the segment in anterograde direction and all values remain unchanged.

\[
\begin{align*}
A_{Pn+1} &= 0, \\
R_{Pn+1} &= 0, \\
A_{Ln+1} &= 0, \\
R_{Ln+1} &= 0, \\
A_{Tn+1} &= > 0, \\
R_{Tn+1} &= 0, \\
C_{Pn+1} &= 0
\end{align*}
\]

The introduction of an impulse from the retrograde side of the segment is in this state always possible. The first element (100) is not refractory and there is also no tail which is conducted in retrograde direction.

Therefore after the introduction of an impulse at element 100 the properties of the segment will be as follows:

\[
\begin{align*}
A_{Pn+1} &= 0, \\
R_{Pn+1} &= 100, \\
A_{Ln+1} &= 0, \\
R_{Ln+1} &= 0, \\
A_{Tn+1} &= > 0, \\
R_{Tn+1} &= RRP, \\
C_{Pn+1} &= 0, \\
S_{Tn+1} &= ST 10
\end{align*}
\]
Finally in the last example the third and most complicated case will be demonstrated.

State 4.

In this state in anterograde direction a refractory tail is being conducted. Behind this tail at the left side a sector of the segment is again excitable. \( \text{AP}_n = 0, \text{AL}_n > 0, \text{AT}_n = 0 \).

Retrogradely there is no impulse nor tail present. There is no collision point. \( \text{RP}_n = 0, \text{RL}_n = 0, \text{RT}_n = 0, \text{CP}_n = 0 \)

\[ \text{ST} \; 4. \quad \text{AP}_n = 0 \; \text{RP}_n = 0 \; \text{AL}_n > 0 \; \text{RL}_n = 0 \; \text{AT}_n = 0 \; \text{RT}_n = 0 \; \text{CP}_n = 0 \]

Independent of the fact whether an impulse can enter the segment in anterograde direction or not, the values indicating the position of the anterograde tail together with those representing the retrograde values and the collision point remain unchanged.

\[ \text{ANT} \; \text{RP}_{n+1} = 0 \; \text{AL}_{n+1} > 0 \; \text{RL}_{n+1} = 0 \; \text{RT}_{n+1} = 0 \; \text{CP}_{n+1} = 0 \]

In this situation one has to check whether an impulse, introduced at element 1, would hit the preceding tail. If so, the impulse will be ignored. If not, the impulse can enter the segment (\( \text{AP}_{n+1} = 1, \; \text{AT}_{n+1} = \text{ARP} \)) and the new state will represent \( \text{ST} \; 5 \).

\[ \text{IF} \; (\text{AL}_{n+1} > (1 + \text{AD})) \]
\[ \text{THEN} : \quad \text{AP}_{n+1} = 1 \]
\[ \quad \text{AT}_{n+1} = \text{ARP} \]
\[ \quad \text{ST}_{n+1} = \text{ST} \; 5 \]
\[ \text{ELSE} : \quad \text{AP}_{n+1} = 0 \]
\[ \quad \text{AT}_{n+1} = 0 \]
\[ \quad \text{ST}_{n+1} = \text{ST} \; 4 \]

In retrograde direction impulse introduction is impossible since element 100 is still refractory. \( \text{AL}_n > 0, \; \text{CP}_n = 0 \).

All values remain unchanged.

\[ \text{RET} \; \text{AP}_{n+1} = 0 \; \text{RP}_{n+1} = 0 \; \text{AL}_{n+1} > 0 \; \text{RL}_{n+1} = 0 \; \text{AT}_{n+1} = 0 \; \text{RT}_{n+1} = 0 \; \text{CP}_{n+1} = 0 \]

2.7 Consequences of short refractory periods and non constant conduction velocity.

So far two major limitations are present in the model.

1: As a result of the definitions chosen, leading to the 3S states the conduction time through a segment is shorter than the refractory period of the segment in the same direction.

2: The conduction velocity of an impulse or tail travelling through a segment is constant as long as the impulse or its tail are present in any part of the segment.
The consequences of these two limitations are as follows:

Limitation 1. A short refractory period

A conduction time through a segment, shorter than the refractory period of that segment, makes it impossible that two impulses will be conducted in one segment in the same direction.

Eliminating this principle will increase the number of possibilities from 35 to almost infinite making acceptable processing impossible.

If the user is confronted with a situation in which the conduction time is only slightly longer than the refractory period the problem can be solved in some situations by lining up multiple segments, each segment having a conduction time equal to the total conduction time divided by the number of subsequent subsegments. All these subsegments will have the original refractory period.

This division of the original segment into subsegments is only possible if the conduction time through the segment is not a function of the rate at which the impulses enter the segment.

![Diagram](image)

**FIGURE 3.7.1.**

Legend to figure 3.7.1.
The division of a segment into two subsegments. T_{segment} represents the conduction time through the segment.
The solution cannot be used if the conduction time through the segment is rate dependent, for example when simulating tissue with decremental conduction properties like the atrioventricular node.
Fig 2.7.2. shows the function curve of a segment where the conduction time of the segment is a function of the input rate.

![Graph showing conduction time vs intervals](image)

**CONDUCTION TIME (ms)**

**REFRACTORY PERIOD**

**INTERVALS (ms)**

**FIGURE 2.7.2.**

Legends to figure 2.7.2.

The shaded area represents that part of the function curve that can be used during the simulation study. In this part the conduction time is smaller than the refractory period. (Mostly the refractory period will also be rate dependent.)

Before an impulse can enter a segment with rate dependent properties, the actual electrophysiological parameters have to be determined. If conduction time is shorter than the refractory period, the segment can be handled as a normal segment with the appropriate conduction time and velocity. The refractory period of the segment can also be defined as rate dependent. In such a situation the segment can be handled as a normal segment if the conduction time at a certain rate is shorter than the refractory period of the segment at that rate. If corrected for the actual rate, the conduction time is not shorter than the refractory period the problem cannot be solved by dividing the segment into subsequent subsegments.

Handling the segment as a normal segment, by dividing the conduction time of the original segment by the number of subsegments (n), the following sub-function curves will apply.
FIGURE 2.7.3.

Legend to figure 2.7.3.
This figure shows a number of rate dependent function curves. The top one (n-1) is defined by the equation:

Conduction time = 500 - cycle length

The other curves are derived from this curve by dividing the conduction time at any rate by 2, 3, 4 or 5.
In figure 2.7.4, 2.7.6, 2.7.8, and 2.7.10, using these function curves, the conduction time through 2, 3, 4 or 5 subsegments is indicated.

During a constant rhythm the division of a rate dependent segment into subsegments does not change the performance of the segment. In the following part at a basic rate of 400 ms the response to a premature impulse at 500 ms is studied.

Using these values, we will show, that the behaviour of a premature impulse depends also on the number of subsegments into which a segment has been divided.

On dividing the segment into n subsegments the time sequence of conduction through these subsegments is as follows.

FIGURE 2.7.4.

Legend to figure 2.7.4.
The segment has been divided into two subsegments. The top segment indicates the conduction time during a regular rate of 400 ms. The bottom one shows the response of the subsegments to a premature impulse after an interval of 300 ms.

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The first subsegment is confronted with a premature impulse with a coupling interval of 300 ms. This results in a conduction time interval of 200/3 = 100 ms. This interval is 50 ms longer than the conduction time during the regular rate of 400 ms. So the prematurity of the premature impulse at the second segment is no longer 100 ms, but 100 ms minus the 50 ms extra delay in the first subsegment. (Interval 350 ms for second segment). This gives a total conduction time of 175 ms.

On dividing the segment into three subsegments, the following situation appears.

\[ \begin{array}{c|c|c}
33.33 & 33.33 & 33.33 \\
66.66 & 55.33 & 48.14 \\
\hline
& & 170.35 \text{ ms}
\end{array} \]

The original segment has been divided into three subsegments. During a regular rhythm of 400 ms the conduction time through the subsegments is 33.33 ms.

The bottom step indicates that a premature impulse requires a longer period to be conducted through the first subsegment. This delay makes conduction through the next subsegment relatively easier because the extra impulse is arriving less prematurely at this and all the following subsegments.
Legend to figure 2.7.7.
The impulse is conducted through the first segment in 200 ms = 66.66 ms. Compared to the conduction time during a regular rate of 400 ms conduction time is 33.33 ms slower. Therefore, the premature at the second segment is 100 minus 33.33 ms (i.e. 66.66 ms). This results in a conduction time through the second segment of 55.55 ms. Finally, this results in a conduction time through the last subsegment of 48.14 ms, giving a total conduction time of 170.55 ms.

After the division in four subsegments the situation is as follows.

<table>
<thead>
<tr>
<th>25</th>
<th>25</th>
<th>25</th>
<th>25</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>43.75</td>
<td>39.06</td>
<td>35.54</td>
</tr>
<tr>
<td>168.35 ms</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Legend to figure 2.7.8.
In the top panel conduction at constant velocity occurs through the four subsegments. Every segment is passed in 25 ms. The bottom panel shows that conduction gradually improves, during conduction through the subsegments.
Legend to figure 2.7.9.
Also in this example the increase in conduction time in a subsegment makes the impulse lost premature in the following subsegment. In every subsegment the conduction time decreases, but the differences in conduction time between two subsegments decrease also.

Division in five parts gives this result.

![Diagram showing conduction time](image)

Legend to figure 2.7.10.
The conduction time per subsegment in the top panel numbers 20 ms. In the bottom panel the same mechanism of reduction in conduction time is shown.
Limitation 2. Non constant conduction velocity

Fig 2.7.12. shows all situations in which an increase in conduction velocity will be in conflict with the limiting criterion no 2, the consistency of the conduction velocity.
The fact that the impulse is handled before the tail makes it possible in these situations that the calculated position of the impulse will be more distal than the position of the tail or even the collision point.

If one of the situations listed here is present the following extra tests must be performed before a segment can be handled in the way previously described.

\[
\begin{align*}
\text{IF } (AL_n - AP_n) \leq AD & \text{ then } AD = (AL_n - AP_n) * 0.99 \\
\text{IF } (RP_n - RL_n) \leq RD & \text{ then } RD = (RP_n - RL_n) * 0.99
\end{align*}
\]

(The value 0.99 has been selected arbitrarily. )

By adding this extra restriction it becomes impossible for the impulse to jump over the tail, i.e. preventing a situation not listed in the 35 possible states. This test only needs to be performed if the AV_{n-1} is not equal to the AV_n, or RV_{n-1} is not equal to RV_n.

By using this restriction in conduction velocity to keep the impulse behind the tail, both the impulse and the tail are conducted within a segment at a fixed minimal distance.

Using the model the frequency of occurrence of this phenomenon is very low. During the simulation studies, described in chapter 3, it never occurred.

If an impulse enters in this way into the next segment three situations are possible.

1) The new segment has the same properties and this state will continue.

2) The refractory period of the new segment is longer and the impulse will block.

3) The refractory period of the new segment is shorter and the gap in between the impulse and the tail increases.

If after a change in conduction velocity, the velocity remains constant, the gap between the impulse and the tail will remain at least 10% of the minimally required distance.

This correction in conduction velocity will be indicated to the user by a statement in the output.
Table 2.7.1 represents the situation that can be reached in any cycle if no extra impulse is entered and the electrophysiological properties remain constant. The columns represent each of the 35 possible states in the $n^{th}$ cycle. Rows represent the possible state in the $(n+1)^{th}$ cycle. A black circle indicates the possible state(s) in which a segment will be found in the $(n+1)^{th}$ cycle, given its state in the $n^{th}$ cycle.
Table 2.7.2. represents the situation that can be reached in any cycle if an extra impulse has entered the segment but the electrophysiological properties remain unchanged.

Like in Table 2.7.1, the columns represent each of the 35 possible states in the (n)th cycle. Rows represent the possible state after the introduction of an impulse.

An black square indicates the possible state(s) in which a segment will be found after the introduction of an impulse given its state in the (n)th cycle.
Table 2.7.3. represents the supplemental situation that can be reached in any cycle if no extra impulse is entered and the electrophysiological properties are allowed unaltered changes (see figure 2.7.12.)

A box in this table, the columns represent each of the 35 possible states in the (n)th cycle. Rows represent the state in the (n + 1)th cycle that corresponds most with the new state.

? indicates the possible state(s) in which a segment will be found in the (n + 1)th cycle, given its state in the (n)th cycle.
Table 2.7.4 represents a compilation of all the the states and data that can be reached in any cycle. The columns represent each of the 35 possible states in the $(n)^{th}$ cycle. Rows represent the possible states in the $(n+1)^{th}$ cycle or after the introduction of an impulse. Circles, squares, and ? have the same meaning as in previous tables.
Chapter 3

Some simulation studies using the model

In this chapter we would like to show the results of some simulation studies performed using the previously described model. First a model of the normal cardiac conduction system of the heart will be designed. We will demonstrate how to define the network, and how to enter the electrophysiological properties of the segments, together with the extra stimuli given.

In the second paragraph a previously published simulation study (47) in which a single purpose mathematical model was used, will be described briefly. The simulation study has been repeated using our model and the results of both methods are compared. As will be shown there is a very good correlation between the original study and the findings using this model.

Finally a more complicated study concerning termination and re-initiation of circus movement tachycardia, due to bundle branch reentry will be described. The last two examples are based on data collected during electrophysiological investigation. Both cases have been published previously (47, 48, 50). In these publications patient data, methods and results are given. To get a better understanding of the mechanisms, responsible for these findings, simulation studies were performed.

3.1 The normal conduction system

![Diagram of the normal conduction system]

**Legend to figure 3.1.1:**
In this figure the catheterizations used are shown. HRA = High Right Atrium, LRA = Low Right Atrium, CS = Coronary Sinus, His = His Bundle position, RP = Right Purkinje System, LP = Left Purkinje System, RV = Right Ventricle, LV = Left Ventricle.

At the right side all junction points and segments are numbered. One direction of conduction is defined to be anterograde (indicated by arrows).
To simulate the behaviour of the cardiac conduction system the following network is assumed to represent a particular physiological situation in man.

After numbering both the junction points and the segments, and defining an anterograde direction in every segment, the model has been defined completely and can be entered into the computer.

To do this, for every junction point, a list of segments, able to conduct from that junction point, together with the direction, must be entered into the computer.

In our example the list has the following format:

<table>
<thead>
<tr>
<th>Junction Point</th>
<th>Segment Number</th>
<th>Direction</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>5</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>6</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>7</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>7</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>7</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>8</td>
<td>9</td>
<td>2</td>
</tr>
</tbody>
</table>

If for instance between junction point 4 and junction point 5 conduction is only possible in the direction of junction point 5, this has to be indicated by skipping the line 5.5.2.

If a network has been stored previously in the memory of the computer, it does not have to be entered again by hand, but can by reloaded by number.

After the selection of the structure of the network and the number of segments, the anterograde and retrograde conduction velocities and refractory periods have to be defined. If a segment is conducting only in one direction, the parameters defining conduction velocity and refractory period in the opposite direction are of no interest.

In the example shown in figure 3.1.1. the following values for conduction time and refractoriness have been selected:
Table 3.1.1.

<table>
<thead>
<tr>
<th>SEGMENT</th>
<th>ATime</th>
<th>RTime</th>
<th>ARP</th>
<th>RRP</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>65</td>
<td>65</td>
<td>250</td>
<td>250</td>
</tr>
<tr>
<td>2</td>
<td>35</td>
<td>35</td>
<td>250</td>
<td>250</td>
</tr>
<tr>
<td>3</td>
<td>40</td>
<td>40</td>
<td>250</td>
<td>250</td>
</tr>
<tr>
<td>4</td>
<td>-80</td>
<td>80</td>
<td>270</td>
<td>270</td>
</tr>
<tr>
<td>5</td>
<td>40</td>
<td>40</td>
<td>250</td>
<td>250</td>
</tr>
<tr>
<td>6</td>
<td>20</td>
<td>20</td>
<td>240</td>
<td>240</td>
</tr>
<tr>
<td>7</td>
<td>45</td>
<td>45</td>
<td>250</td>
<td>250</td>
</tr>
<tr>
<td>8</td>
<td>25</td>
<td>25</td>
<td>240</td>
<td>240</td>
</tr>
<tr>
<td>9</td>
<td>20</td>
<td>20</td>
<td>240</td>
<td>240</td>
</tr>
</tbody>
</table>

Legend to table 3.1.1.

ATime and RTime represent the antegrade and retrograde conduction time. ARP and RRP the antegrade and retrograde refractory period. All times are in ms.

One sees that segment number 4 representing AV Nodal conduction has been given a negative conduction time.

This has been done for two reasons:

Firstly the negative sign indicates, that the parameter is not constant, but has a rate dependent conduction time.

Secondly, the value behind the minus sign indicates the conduction time in the first pass through the segment. At that moment, because it is the first pass, the rate at the junction point cannot be determined.

The rate dependent properties of the segment are questioned after the selection of all parameters.

To describe the relation between the rate and the conduction velocity, the two variables a and b in the equation

Conduction time = a * Rate + b

have to be entered.

In this example the selected values are: a = -0.2 and b = 200.

In the same way, rate dependent refactoriness can be defined.

After the selection of the network and the electrophysiological properties of the segments, the mathematical model of the conduction system is ready to perform a simulation study.

To start such a simulation study, one or more impulses should be entered into the not activated network. To do so, two methods are presently available:

a. First one can induce a basic rhythm of a certain duration, defined by its starting point in time, the interval and its end point in time, together with the
junction point at which the impulses have to be entered into the network. At multiple junction points regular rhythms can be induced.
b. Secondly one can select single stimuli and use them either combined with a basic rhythm as an extra stimulus or just as a single impulse. Again, multiple extra stimuli can be selected, either at the same or at different junction points.

The basic rhythm and the extra stimuli are finally chronologically listed. After every simulation cycle, (in general every millisecond), the clock of the model is compared with the list of points of time previously composed. If they match, at the corresponding junction point an impulse is introduced. The conditions this impulse has to fulfill to be conducted into the segment have been described in chapter 2, paragraph 6.

c. Thirdly before the actual simulation study starts, the state of one or more segments can be selected to be unequal to zero.

In that case the following parameters have to be defined:

AD, RD, AL, RL, AT, RT, and ST

In this way one can create artificially the situation present after the introduction of an impulse exclusively in one segment. Although theoretically possible it is less useful to introduce in this way, both an anterogradely and a retrogradely conducted impulse. The state of multiple segments can be changed in this way.

In the study demonstrated in this example, the following pulse train has been used.

A basic rate starting at point t=20, with an interval of 600 ms has been selected introducing two impulses. These basic impulses (t=620 and t=1220 ms) are followed by one premature impulse after 1620 ms. After a compensatory pause the regular rhythm continues after 2420 ms.

All impulses are given at junction point 1.

The last question to be answered is the time (in milliseconds), that the simulation process has to be continued. After this input, the program starts to simulate conduction through the network.

In most cases the following output layout has been selected:

<table>
<thead>
<tr>
<th>Junction point</th>
<th>Time of appearance</th>
<th>From segment</th>
</tr>
</thead>
<tbody>
<tr>
<td>xxx</td>
<td>xxx</td>
<td>xxx</td>
</tr>
</tbody>
</table>

The values are shown on a monitor and/or a line printer.

Using the network described in figure 3.1.1. and the parameters listed in table 3.1.1., the reaction of the model on the above described pulse train will be demonstrated.
Table 3.1.2 gives the output after a simulation time of 3000 ms.

Legend to figure 3.1.2.
At time t=0 the first impulse is introduced into junction point 1. This point represents a position high in the right atrium, near the atrioventricular node. The impulse conducts through the atrium, through the AV node in 60 ms and over the two bundle branches to the ventricle.
At t=620 a second impulse is introduced and conducts in the same way through the conduction system. A third impulse is given at t=1220. At t=1620 a fourth impulse is introduced. This impulse will reach the AV node in a premature manner and result in an AV nodal conduction time of 150 ms. The conduction through the rest of the conduction system is identical as in the previous tests. After this premature impulse, a compensatory pause is present. So at t=2420, the next atrial impulse appears at junction point 1. This measured from the previous impulse delayed impulse will conduct fast through the AV node in 40 ms. The rest of the conduction system is passed in the usual way.
The following regular impulses will be handled like the first impulse.

NB: In this and following examples sometimes an error of 1 ms can be observed. The reason for this error will be explained in chapter 4.

3.2. Cycle length alternation.

In 1981 we studied the possible role of the AV Nodal function curve as a cause of cycle length alternation, during circus movement tachycardia (47-48). In these publications two types of AV nodal function curves during tachycardia were used: straight lines of various gradients and representative examples of patient-based AV nodal function curves obtained during clinical electrophysiologic investigations. This was done using a mathematical model of the tachycardia circuit loaded into an Apple II microcomputer. In this model the following assumptions were made:

\[ AA = \text{the tachycardia cycle length} \]
\[ AH = \text{the conduction time through the AV Node and} \]
\[ K = \text{the conduction time through the rest of the circuit. This conduction time was assumed to be constant and rate independent.} \]

and the following basic equation was defined:

\[ AA = AH + K \]

The relation between the atrial rate and the AV Nodal conduction time - the AV Nodal function curve - was varied and the resulting tachycardia was studied. During circus movement tachycardia a fixed point on the AV Nodal function
curve was used, resulting in a constant tachycardia cycle length. A premature
impulse given at the atrial side of the AV Node, would shorten the cycle length.
This would cause an increase in conduction time through the AV Node. This
prolonged conduction time, together with the constant conduction time K through
the rest of the circuit formed the new cycle length. This cycle length would be
longer than during regular tachycardia. This would cause a faster conduction
through the AV Node. The circulating impulse arrived premature at the AV Node
and so on.

To study the effect of different AV Nodal function curves upon the tachycardia
cycle length, in that model two groups of function curves were applied:

- Simple first degree polynomials representing the conduction through the AV
  Node as a function of the stimulus interval. Different slopes could be selected.
- Patient based AV Nodal function curves. These curves were obtained during
  clinical electrophysiological studies using the extra stimulus technique.
  An extra stimulus was given in the atrium during a regular paced rhythm.
  These patients showed cycle length alternation during these investigations.

Using a straight-line relationship between rate and conduction time, three different
groups were selected.

a) Straight line AV Nodal function curves with a gradient = -1
   \[ \text{(Slope} = -1\) \]

b) Straight line AV Nodal function curves with a gradient > -1
   \[ \text{(Slope} < -1\) \]

c) Straight line AV Nodal function curves with a gradient < -1
   \[ \text{(Slope} > -1\) \]

The effect of a shortening of the stimulation interval on a tachycardia cycle was
studied, using these three different groups.

Secondly patient based function curves were used. Similar findings could be
obtained in simulation studies using these patient-based curves. The result of a
perturbation of the tachycardia cycle length depended on the slope of the function
curve in that point, representing the instantaneous AA interval.

The determination of the relation between the gradient of the AV Nodal function
curve, the perturbation of the original tachycardia cycle length and the resulting
cycle length alternation, has been repeated using the in chapter 2 described
mathematical model of the cardiac conduction system. The results are identical
as compared to the findings in the original study.
The network used in this study contains four segments.

**Legend to figure 3.2.1**
Model representation of the study of a circus movement tachycardia. It is however possible to represent the conduction through segments 1, 2 and 3 using only one segment considering the refractory period of this new segment is longer than the conduction time through all three segments together.

The following network structure and electrophysiological parameters were entered.

**Table 3.2.1.**

<table>
<thead>
<tr>
<th>JP</th>
<th>Segment</th>
<th>A/R</th>
<th>AD</th>
<th>RD</th>
<th>ARP</th>
<th>RRP</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>1</td>
<td>R</td>
<td>1.25</td>
<td>200</td>
<td>200</td>
</tr>
<tr>
<td>1</td>
<td>4</td>
<td>2</td>
<td>1.25</td>
<td>200</td>
<td>200</td>
<td>200</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>2</td>
<td>1.25</td>
<td>200</td>
<td>200</td>
<td>200</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>4</td>
<td>1.25</td>
<td>200</td>
<td>200</td>
<td>200</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Legend to table 3.2.1**
JP = Junction Point, A/R: 1 = Anterograde, 2 = Retrograde.
AD and RD represent the number of elements passed in one cycle. ARP and RRP are the refractory periods.
R = Rate dependent. In this example the curve has been described by the equation $AH = AA + 400$.

The circulating impulse is introduced into the circuit by changing the state and properties of one segment of the network before the simulation starts.

At position one in segment one an impulse is introduced. By introducing it exclusively in one direction in this segment, and not at the adjacent junction point, a circus movement tachycardia starts.
The results:

Straight line AV nodal function curve with a gradient = -1.

Table 3.2.2 shows the effect of perturbation of a circus movement tachycardia using an AV Nodal function curve with a gradient of -1.

| J POINT 2 TIME 80 FROM SEGMENT 1 | J POINT 1 TIME 1248 FROM SEGMENT 4 |
| J POINT 1 TIME 108 FROM SEGMENT 2 | J POINT 2 TIME 1258 FROM SEGMENT 2 |
| INTERVAL = 238 |
| J POINT 1 TIME 328 FROM SEGMENT 4 |
| J POINT 2 TIME 480 FROM SEGMENT 1 |
| J POINT 2 TIME 480 FROM SEGMENT 2 |
| J POINT 4 TIME 568 FROM SEGMENT 3 |
| INTERVAL = 246 |
| J POINT 1 TIME 600 FROM SEGMENT 3 |
| INTERVAL = 282 |
| J POINT 1 TIME 719 FROM SEGMENT 1 |
| J POINT 3 TIME 719 FROM SEGMENT 2 |
| INTERVAL = 299 |
| J POINT 1 TIME 959 FROM SEGMENT 4 |
| INTERVAL = 357 |
| J POINT 2 TIME 1800 FROM SEGMENT 1 |
| J POINT 2 TIME 2227 FROM SEGMENT 1 |
| J POINT 4 TIME 1168 FROM SEGMENT 3 |
| INTERVAL = 201 |

**TABLE 3.2.2.**

![Cycle Length vs. Beat Number](image)

**FIGURE 3.2.2.**

Legend to Table 3.2.2 and Figure 3.2.2.
The net result is a stable cycle length alternation with an amplitude equal to the initial perturbation. This alteration will last indefinitely unless the AV Nodal conduction properties change.

Straight line AV Nodal function curve with a gradient > -1.

Using the same network and electrophysiological parameters the function curve has been rotated to a more flat position. The new curve has been described by the equation

\[ AH = -0.5 \times AA + 240 \]

At the rate of the regular tachycardia (320 ms) it represents the same AV Nodal conduction time as in the first example, i.e. 80 ms.
TABLE 3.2.3.

<table>
<thead>
<tr>
<th>POINT</th>
<th>TIME FROM SEGMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>60</td>
</tr>
<tr>
<td>3</td>
<td>100</td>
</tr>
<tr>
<td>4</td>
<td>150</td>
</tr>
<tr>
<td>5</td>
<td>200</td>
</tr>
<tr>
<td>6</td>
<td>250</td>
</tr>
</tbody>
</table>

INTERVAL = 350

<table>
<thead>
<tr>
<th>POINT</th>
<th>TIME FROM SEGMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>56</td>
</tr>
<tr>
<td>2</td>
<td>102</td>
</tr>
<tr>
<td>3</td>
<td>148</td>
</tr>
<tr>
<td>4</td>
<td>194</td>
</tr>
<tr>
<td>5</td>
<td>240</td>
</tr>
<tr>
<td>6</td>
<td>286</td>
</tr>
</tbody>
</table>

INTERVAL = 250

<table>
<thead>
<tr>
<th>POINT</th>
<th>TIME FROM SEGMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>144</td>
</tr>
<tr>
<td>2</td>
<td>189</td>
</tr>
<tr>
<td>3</td>
<td>235</td>
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<tr>
<td>4</td>
<td>281</td>
</tr>
<tr>
<td>5</td>
<td>327</td>
</tr>
</tbody>
</table>

INTERVAL = 200

<table>
<thead>
<tr>
<th>POINT</th>
<th>TIME FROM SEGMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>232</td>
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<tr>
<td>2</td>
<td>278</td>
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<tr>
<td>3</td>
<td>324</td>
</tr>
<tr>
<td>4</td>
<td>370</td>
</tr>
<tr>
<td>5</td>
<td>416</td>
</tr>
<tr>
<td>6</td>
<td>462</td>
</tr>
</tbody>
</table>

INTERVAL = 168

<table>
<thead>
<tr>
<th>POINT</th>
<th>TIME FROM SEGMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>320</td>
</tr>
<tr>
<td>2</td>
<td>366</td>
</tr>
<tr>
<td>3</td>
<td>412</td>
</tr>
<tr>
<td>4</td>
<td>458</td>
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<tr>
<td>5</td>
<td>504</td>
</tr>
<tr>
<td>6</td>
<td>550</td>
</tr>
</tbody>
</table>

INTERVAL = 280

<table>
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<th>TIME FROM SEGMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>500</td>
</tr>
<tr>
<td>2</td>
<td>546</td>
</tr>
<tr>
<td>3</td>
<td>592</td>
</tr>
<tr>
<td>4</td>
<td>638</td>
</tr>
<tr>
<td>5</td>
<td>684</td>
</tr>
<tr>
<td>6</td>
<td>730</td>
</tr>
</tbody>
</table>

INTERVAL = 424

<table>
<thead>
<tr>
<th>POINT</th>
<th>TIME FROM SEGMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>688</td>
</tr>
<tr>
<td>2</td>
<td>734</td>
</tr>
<tr>
<td>3</td>
<td>780</td>
</tr>
<tr>
<td>4</td>
<td>826</td>
</tr>
<tr>
<td>5</td>
<td>872</td>
</tr>
<tr>
<td>6</td>
<td>918</td>
</tr>
</tbody>
</table>

INTERVAL = 232

<table>
<thead>
<tr>
<th>POINT</th>
<th>TIME FROM SEGMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>904</td>
</tr>
<tr>
<td>2</td>
<td>950</td>
</tr>
<tr>
<td>3</td>
<td>996</td>
</tr>
<tr>
<td>4</td>
<td>1042</td>
</tr>
<tr>
<td>5</td>
<td>1088</td>
</tr>
<tr>
<td>6</td>
<td>1134</td>
</tr>
</tbody>
</table>

INTERVAL = 232

FIGURE 3.2.3.

Legend to table 3.2.3 and figure 3.2.3:
A 50 ms prematurely given impulse at t = 560 instead of t = 640 results in cycle length alternation, that damps out rapidly, exactly as expected.

Straight line AV Nodal function curve with a gradient < 0.1.

Using the same network and parameters for the third time, the experiment has been repeated using a steep AV Nodal function curve. With the use of this curve defined by:

\[ \text{AH} = -1.5 \times AA + 560 \]

the reaction of the tachycardia cycle length on a perturbation of the rate has been studied.
This curve represents a rotation of the AV Nodal function curve using the same rotation point (AA=320, AH=80) as in the two previous examples.

| J POINT 1 | TIME 102 FROM SEGMENT 1 | J POINT 2 | TIME 210 FROM SEGMENT 2 |
| J POINT 3 | TIME 248 FROM SEGMENT 3 | J POINT 4 | TIME 318 FROM SEGMENT 4 |
| J POINT 5 | TIME 568 FROM SEGMENT 5 | J POINT 6 | TIME 648 FROM SEGMENT 6 |
| J POINT 7 | TIME 688 FROM SEGMENT 7 | J POINT 8 | TIME 930 FROM SEGMENT 8 |

**TABLE 3.2.4.**

![Graph](image)

**FIGURE 3.2.4.**

Legend to Table 3.2.4: and Figure 3.2.4.
A premature impulse with a prematurity of only 10 ms starts the alternation of the tachycardia cycle length. The amplitude of the perturbation increases and the tachycardia stops after finding one of the segments of the circuit still refractory.

In all these experiments the results are identical to those found using the single purpose model. (47-48)

3.3 Circumvovement tachycardia and the WPW syndrome.

In the last example performed to demonstrate the behavior of this mathematical model, a combination was made of a branching network and an accessory pathway. (see figure 3.3.1.)

In 1980 we studied a patient with intermittent Wolf-Parkinson-White syndrome and bundle branch reentry, in whom different mechanisms of block of impulse propagation in several reentrant circuits resulted in a major discordance between the "echo-zone" and the "tachycardia-zone". (50) It illustrates the delicate balance in electrophysiological parameters of the segments incorporated in reentry circuits required to initiate and sustain the arrhythmia and the interaction of multiple reentry circuits.

Based on the data found during this investigation a simulation study was performed to explore the relations between conduction velocity, refractory period and the structure of the reentry circuit.
FIGURE 3.3.1.

Legend to figure 3.3.1. This figure shows the network representing parts of the conduction system of the heart together with an accessory pathway between the ventricle and the atrium on the left side of the heart. The junction points represent the following anatomical sites: 1 = Low Right Atrium, 2 = His Bundle, 3 = Left Ventricle, 4 = Coronary Sinus, 5 = Right Ventricle.

The segments represent: 1 = AV Node, 2 = Left Bundle, 3 = Accessory Pathway, 4 = Trans Atrial Conduction, 5 = Right Bundle, 6 = Transepithelial Conduction.

The segments in this network have the following properties:

<table>
<thead>
<tr>
<th>Segment</th>
<th>ATime</th>
<th>RTime</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>R</td>
<td>100</td>
</tr>
<tr>
<td>2</td>
<td>80</td>
<td>80</td>
</tr>
<tr>
<td>3</td>
<td>80</td>
<td>80</td>
</tr>
<tr>
<td>4</td>
<td>80</td>
<td>80</td>
</tr>
<tr>
<td>5</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>6</td>
<td>40</td>
<td>40</td>
</tr>
</tbody>
</table>

The refractory periods of these segments are at the beginning of the study so short, that the impulse during circus movement tachycardia never finds a refractory segment in front of it. On the other hand the refractory periods are so long that they are not in conflict with the definitions given in chapter 2 paragraph 7.

During the simulation study the influence of the duration of some refractory periods on the tachycardia will be studied.
At the beginning of the study there is a circus movement tachycardia using segment 1 representing the AV Node, anterogradely and segment 3, representing the accessory pathway, retrogradely.

The circus movement tachycardia has a rate of 320 ms, which includes an AV Nodal conduction time of 80 ms.

FIGURE 3.3.2.

Legend to figure 3.3.2.

Figure 3.3.2. represents the first revolution of the impulse through the circuit composed of the AV Node, the left bundle, the accessory pathway, and the atrium.
Legend to figure 3.3.3.

Figure 3.3.3. shows the second revolution.

After 320 ms the circuit has been closed once and the impulse starts its second revolution. The impulse will conduct through the AV Node in the same time and would reach junction point 1 again after 320 ms at t= 640. But 40 ms earlier, at t=600 a premature impulse has been given at junction point 1.

Legend to figure 3.3.4.

This impulse will conduct retrogradely through segment 4 and collide with the circulating impulse. In antegrade direction the premature impulse will conduct through segment 1, representing AV Node conduction. Since it is premature the conduction time through the segment is prolonged to 120 ms. The conduction through segment 3,3 and 4 is rate independent, so the impulse will reach the junction point 1 with the same delay of 40 ms.
FIGURE 3.3.3.

Legend to figure 3.3.3:
This results in a conduction time through segment 1 of 40 ms, with the impulse arriving at junction point 2 at t=1000. Junction point no 2 has been activated previously at t=700. If the anterograde refractory period of segment 2 is selected to be 310 ms, the impulse is not able to penetrate into this segment and left bundle branch block will occur. The impulse is able to enter segment 5 acrossing the right ventricle and reaching the left ventricle 40 ms later over the interventricular septum.

From junction point 3, segment 2 is activated retrogradely, at the same time the impulse continues to conduct through the accessory pathway retrogradely to the atrium.

Depending on the selected refractory periods in segment no 1 and no 5, the following situation can be simulated:

- If segment 1 is no longer refractory, the impulse will conduct retrogradely and collide with the circulating impulse.
- If the refractory period of segment 5 is sufficiently short in anterograde direction, the impulse can conduct again to junction point 5. If no block occurs in the following segments the circus movement tachycardia will be reinitiated.
TABLE 3.3.1.

<table>
<thead>
<tr>
<th>Point</th>
<th>Time (ms)</th>
<th>Segment</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>100</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>140</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>240</td>
<td>3</td>
</tr>
<tr>
<td>1</td>
<td>336</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>320</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>400</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>480</td>
<td>6</td>
</tr>
<tr>
<td>4</td>
<td>500</td>
<td>7</td>
</tr>
<tr>
<td>6</td>
<td>600</td>
<td>8</td>
</tr>
<tr>
<td>7</td>
<td>729</td>
<td>9</td>
</tr>
<tr>
<td>8</td>
<td>779</td>
<td>10</td>
</tr>
<tr>
<td>9</td>
<td>879</td>
<td>11</td>
</tr>
<tr>
<td>10</td>
<td>1059</td>
<td>12</td>
</tr>
<tr>
<td>11</td>
<td>1199</td>
<td>13</td>
</tr>
<tr>
<td>12</td>
<td>1289</td>
<td>14</td>
</tr>
<tr>
<td>13</td>
<td>1349</td>
<td>15</td>
</tr>
<tr>
<td>14</td>
<td>1359</td>
<td>16</td>
</tr>
</tbody>
</table>

**FIGURE 3.3.6.**

Legend to table 3.3.1 and figure 3.3.6.

Table 3.3.1 contains the computer output as described in this paragraph. Figure 3.3.6 shows the ladder diagram derived from this table.

The time of activation of the different junction points is given, together with the segment they may be considered to have passed through at that time. The last considered impulse conducted through the AV node is 1.2 ms after the preceding impulse. The first considered impulse conducted through the AV node is 70 ms after the preceding impulse. Both ventricles are activated via the bundle branches of the bundle of His. The left bundle branch is activated via the right bundle branch through the atrioventricular septum and retrogradely through the left bundle branch. At the same time, the impulse is conducted through the atrioventricular septum and reaches the left atrium at 1.18 s. The total cycle length of this cycle becomes 3.01 s. After being conducted through the AV node in 68 ms the impulse finds the left bundle branch again refractory due to the retrograde conduction. After the retrograde conduction time of 1.9 ms the impulse is conducted through the right bundle branch and retrogradely through the left bundle branch. The retrograde conduction time of the AV node conduction also results in an increase in the cycle length of 308 ms. The AV nodal conduction time in the next cycle shortens to 41 ms and the impulse is conducted again over the right bundle branch. The retrograde conduction time of the AV node conduction time in the next cycle shortens to 41 ms and the impulse is conducted again over the right bundle branch. The retrograde conduction time of the AV node conduction time in the next cycle shortens to 41 ms and the impulse is conducted again over the right bundle branch. But now the left bundle branch is still refractory and does not become penetrated retrogradely in the cycle. In the next cycle starting from 1.182 s both bundle branches are able again to conduct the impulse retrogradely and a "normal" cycle with a cycle length of 308 ms resumes. Junction point 2 has been activated at 1.182 s and is now activated at 1.226 s. The interval is shorter as the refractory period of the left bundle branch and another beat that left bundle branch block will occur. The impulse penetrates the left bundle branch retrogradely and junction point 2 is reached at 1.250 s. In the next revolution of the cycle the impulse junction point 2 is reached at 1.250 s.
Chapter 4.

General discussion

In this chapter the following subjects will be discussed:

A. The limitations of mathematical simulations in general and in our model in particular.
B. The relation between the time required for a complete simulation study and the resulting accuracy.
C. The problems and possibilities of the use of the model in real time during clinical electrophysiological investigations.
D. Clinical applications
E. Didactical aspects of the use of a mathematical model to simulate electrophysiological phenomena in man.

A. The limitations of mathematical simulations in general and in our model in particular.

No matter how accurately a mathematical model has been designed, simulation remains an imitation of reality. Often many relations between different parameters are unknown or not constant in time. Nevertheless the known relations are assumed to represent the behaviour of the different parts of the model.

Every mathematical model designed for simulation purposes, has its own structure and inherent errors. The number and type of errors depends upon the details of the structure of the model. These errors are additional to those introduced because some parameters and relations between parameters may be unknown.

In this model one of the main sources of error results from the fact that the number of elements in each segment is not unlimited. An unlimited increase in the number of elements in each segment would make it impossible to simulate even very simple processes in a short period of time.

In the present model the number of elements over which an impulse travels during one simulation cycle is calculated by dividing the number of elements in each segment (100) by the conduction time in ms.

However an impulse in this model starts at element 1. Conduction through a segment is assumed to have finished when element 100 is reached or passed. It makes no difference whether during the last simulation cycle the impulse just reaches element 100 or passes it (and conducts to an element located more distal than this theoretically last element). This means that only 99 elements are passed in each segment. The error introduced by this fact means that the conduction time resulting from a simulation study can either be greater or smaller than the conduction time selected at the beginning of a simulation study. One way of
controlling this error is to select conduction times less than 100 ms. Then the difference between selected and actually simulated conduction time will remain smaller than 1 ms per segment.

Another method to control error in calculation of conduction time is to start an impulse at element 0. In such a situation the conduction time calculated during the simulation study would always be equal to or longer than the interval selected at the beginning of a study.

A third possible method to overcome this inaccuracy is the following: The fact that only 99 elements must be passed can be compensated by compensating the selected conduction times through a segment by a factor 0.99. The simulation time interval derived using this correction factor is in this situation also equal to or longer than the initially selected values.

Using one of the last two methods, the following error will occur:

If an impulse conducts through a network built of segments with rate independent conduction times, the conduction time through every segment will increase, compared to the actually selected values. The intervals in the mathematical model will vary from those in reality.

In the present model some errors in conduction time will be greater and some smaller than the ones initially selected. The accumulative effect of these errors will tend towards zero.

The following calculations illustrate the magnitude of the error introduced by these three different methods.

Using 91 different selected conduction velocities, \( V_{sel} \), starting at 1.0 element/ ms, increasing in 0.1 ms steps upto 10.0 elements/ ms, the following parameters have been calculated.

\[ T_{sel} \] The initially selected conduction time through the segment.

\[ T_{sel} = \frac{100}{V_{sel}} \]

\[ T_{sys99} \] The simulated conduction time required to conduct an impulse over 99 segments using the definitions described in chapter 2. This is the time necessary to conduct from element 1 to element 100.

\[ T_{sys100} \] The conduction time required to conduct the impulse over 100 elements.

\[ T_{sys99/100} \] The corrected conduction time required to conduct an impulse over 99. The conduction velocity of the impulse has been multiplied by a factor 0.99.

\[ D1 \] The difference between the theoretical conduction time \( T_{sel} \) and the simulated conduction time \( T_{sys99} \)

\[ D2 \] The difference between the theoretical conduction time \( T_{sel} \) and the simulated conduction time \( T_{sys100} \)

\[ D3 \] The difference between the conduction time \( T_{sys99} \) and the corrected conduction time \( T_{sys99/100} \)
Calculation of the mean over these 31 subsequent values gives the following error:

\[ D_1 = 0.248 \]

\[ D_2 = -0.457 \]

\[ D_3 = -0.490 \]

Fig. 4.11 shows an example of this situation. One sees a network containing four segments. Together they form a re-entry circuit in which an impulse is circulating clockwise. All values mentioned are derived in the direction of the circulating impulse.
<table>
<thead>
<tr>
<th>SEGMENT</th>
<th>Vsel</th>
<th>Tsel</th>
<th>Tsys69</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>100</td>
<td>99</td>
</tr>
<tr>
<td>2</td>
<td>1.5</td>
<td>66.6</td>
<td>66</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>50</td>
<td>50</td>
</tr>
</tbody>
</table>

**FIGURE 4.1.1.**

Legend to figure 4.1.1. This figure shows a re-entry circuit containing four segments. Vsel indicates the selected conduction velocity in elements / simulation cycle. Tsel represents the initially selected conduction time, and Tsys69 shows the conduction time calculated by the model. Note that all conduction velocities are constant and not rate dependent.

**Time required to perform one cycle:**

Theoretically: 236.66 ms

Using $T_{sys69}$: 235.00 ms

The revolution time is slightly shortened, but remains constant.

In another example, we will study the behavior of the same network, after replacing segment 1, by a segment with a rate dependant conduction time. The properties of this segment are equal to the segment used in paragraph 3.2.
FIGURE 4.1.2.

Legend to figure 4.1.2. In this example the conduction time through segment 1 is rate dependent. The relation between the rate and the conduction time is indicated in the left side of the figure.

The conduction time in the direction of the tachycardia in the other segments is as follows:

<table>
<thead>
<tr>
<th>Segment</th>
<th>ATime</th>
<th>RTime</th>
<th>AD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Rate</td>
<td>Rate</td>
<td>Rate All values</td>
</tr>
<tr>
<td></td>
<td>Dependent</td>
<td>Dependent</td>
<td>Dependent measured in ms.</td>
</tr>
<tr>
<td>2</td>
<td>80</td>
<td>80</td>
<td>1.25</td>
</tr>
<tr>
<td>3</td>
<td>80</td>
<td>80</td>
<td>1.25</td>
</tr>
<tr>
<td>4</td>
<td>80</td>
<td>80</td>
<td>1.25</td>
</tr>
</tbody>
</table>

Through this circuit an impulse is circulating clockwise having a revolution time of 320 ms. By giving a premature impulse at junction point 1, the activation interval of segment 1 shortens to 280 ms. Immediately this will cause a prolongation of the conduction time through this segment of 40 ms to 120 ms. This results in a revolution time of 359 ms causing an acceleration of the conduction velocity resulting in a conduction time through segment 1 of 41 ms. Theoretically this process can continue indefinitely.

After entering this network, the conduction times and refractory periods and the previously mentioned impulses the computer will generate the following output listing. (t=0 indicates the introduction of the premature impulse in segment no 1.)
### TABLE 4.1.2.

Legend to table 4.1.2.

This reproduction of the computer output shows the junction point reached by an impulse, the time of occurrence and the segment lastly used by this impulse.
The difference between the theoretical cycle length and the calculated one is drawn in figure 4.1.3.

![Diagram showing cycle length comparison](image)

Legend to figure 4.1.3:
The figure demonstrates that the difference between the calculated simulation time and the theoretically selected time interval is not constant. As a result of a rate-dependent segment in the network, the error between expected and simulated circuit time increases after every revolution through the network. After 1500 ms the model is stable and alternates around the tachycardia cycle length with an amplitude of 10 ms and a fixed difference of 21 ms.

B. The relation between the time required for a complete simulation study and the resultant accuracy.

The model described herein was developed using the Basic computer language and an Apple II microcomputersystem.

During the design of the model the use of this interpreter level language was selected, because program changes could be made easily. One of the big disadvantages of this interpreter level language is its relatively slow calculation velocity. To overcome this problem the model was translated from Basic to Fortran to be used on a VAX370 computer system.

Using this compiler level language instead of Basic, the calculation velocity increased by a factor of approximately 100.

Independent of the selected computer language, the time necessary to simulate a certain process consists of two parts:

The first part indicates
a) the time to define the structure of the network,
b) the time to define the properties of the different segments and the impulses,
c) the time required to produce the results and

d) the usertime (i.e. the time elapsed while the system waits for user input).

The second part depends on
a) the number of cycles that has to be simulated,
b) the number of segments involved,
c) the state of these segments and
d) the desired accuracy.
If one desires to increase the temporal resolution from 1ms / segment to 0.1 ms / segment, this goal can be reached by increasing the number of elements in one segment from 100 to 1000 and by multiplying the conduction velocity by 0.1.

Since this increase in accuracy will not greatly influence time for definition of the network etcetera, the total simulation time will increase by a factor smaller than 10.

Unless one wants to simulate very small segments it is seldom necessary to obtain a temporal resolution of less than 1 ms. The inaccuracy of obtaining input data is in most cases a multiple of the error caused by the number of elements.

C. The problems and possibilities of the use of the model in real time during clinical electrophysiological investigations

One of the most fascinating areas to use this mathematical model is during clinical electrophysiological investigation in man. To make it possible to work in the electrophysiology laboratory the following criteria must be fulfilled. First it would be necessary to have all values required available during the study. Attempts have been made to develop computer systems to detect the potentials at different sites in the heart and to measure conduction intervals between these sites (51). Many of these systems are able to detect reliable and reproducible potentials during regular rhythms. None of these systems is able to provide the required intervals during the invasive electrophysiological study. During complex arrhythmias automatic calculations of intervals are unreliable and not suitable for use as input in a computer model of conduction in a real time situation.

A second condition that has to be fulfilled is the following. To be able to use the model in real time the simulation velocity must be increased. The time required to simulate a certain process has to be of the same magnitude as the process itself.

If both criteria would be fulfilled, it may be possible for instance to use the computer during the electrophysiological study of patients with tachycardia. Based on the clinical data the model could predict the effect of extra stimuli at different times and locations. These data may be of importance for terminating circus movement tachycardias. Also for the evaluation of programmable permanent pacemakers the model could be a helpful instrument.

At present the criteria required to make these applications possible have not yet been fulfilled. Hopefully in the near future it will become possible to use the model during the electrophysiological investigations as described above.

Two areas where the model can be used already with much success will be described in the following paragraphs.

D. Clinical applications

To initiate clinical circus movement tachycardia three conditions have to be fulfilled:
- A circuit has to be available
- Unidirectional block has to be present.
- Conduction in the circuit has to be slow enough to find excitable tissue ahead of the impulse.

In our mathematical model all these criteria can be realized. Using the model the following clinical aspects of reentrant tachycardia have been studied.

- The influence of the prematurity of the extra stimulus on initiation and termination of reentrant tachycardias. In chapter 3.3 an example of the simulation of termination of a reentrant tachycardia by giving an extra stimulus has been discussed.

- The effect of the administration of medication on a reentrant tachycardia. To do so the influence of this drug on the conduction velocity, ability to conduct and the refractory period of one or more segments has to be defined. Because the model has an internal clock all these parameters can be defined as being time dependent.

In chapter 3.2 the role of the AV nodal function curve as a possible cause of cycle length alternation has been discussed. In a publication describing this relation, the influence of medication on the tachycardia cycle length has also been studied.(47) By movement of the AV nodal function curve to the right, cycle length alternation could be initiated. Movement of the AV nodal function curve in this direction occurs during administration of drugs that increase AV nodal refractoriness. This could explain why these drugs often induce clinical cycle length alternation. Induction of cycle length alternation in the tachycardia model by gradual movement of the AV nodal refractory curve to the right tends to cause a gradual onset of alternation, with a gradual increase in amplitude. This is frequently seen in clinical cycle length alternation.

Finally the influence of the site of stimulation on initiation and termination of reentrant tachycardia can easily been studied. By decreasing the conduction velocity of a segment connecting the site of stimulation and the tachycardia circuit a greater distance can be simulated. The way a second extra impulse abbreviates the time required to terminate a tachycardia can easily be demonstrated. Recently our group published an article to illustrate the mechanisms causing this phenomenon (52).

E. Didactical aspects of the use of a mathematical model to simulate electrophysiological phenomena in man.

This model which was originally designed as an instrument for research in clinical electrophysiology, can also be used for teaching. Education by simulation models offers some important advantages to the student. Independent of the teacher the student can repeat experiments as often as wanted. With each experiment it is possible to change one or more parameters and to study the response of the model to the new conditions.
In the present model some built-in networks are available. The student can study basic electrophysiology such as the properties of the normal cardiac conduction system, conditions required for reentry, and the initiation and termination of reentry tachycardias with programmed extrastimuli.

But these teaching facilities are not limited to the student. Also investigators can use these mathematical models as an objective judge to test their knowledge and understanding.

We believe therefore that the use of simulation models should not be limited to some areas in medicine where it has been accepted already. It deserves to be applied on a much wider scale.
Chapter 5.

Summary
Samenvatting
Rizzumee

Summary
This study describes a mathematical model of the conduction system of the heart. Using this model it is possible to simulate reentrant tachycardias. Also the influence of extra stimuli and drugs on these tachycardias can be studied. In this way hypotheses can be tested, concerning the mechanism of reentrant tachycardias initiated during programmed electrical stimulation of the heart. In chapter one a short introduction is given to the history of research concerning the causes of rhythm disturbances of the heart. Further a number of simulation models used in cardiac electrophysiology has been reviewed. Finally this chapter ends with an overview of the criteria this model has to fulfil.

In chapter two a description of the model is presented. It includes the layout of the model, a description of the parts (segments) used to build the model and a contemplation about the order in which the conduction of an impulse through a segment has to take place. Also in this chapter the equations describing the conduction of an impulse through a segment and the introduction of an impulse into a segment have been illustrated. Finally the consequences of some limitations of the model are discussed.

In chapter three three simulation studies are illustrated. The simulation of the normal conduction system of the heart, followed by the simulation of a reentrant tachycardia in a patient with the WPW Syndrome. In the third study an example is given about how a hypothesis derived during clinical investigation, concerning the mechanism of the tachycardia, can be tested.

In chapter four special attention is given to the limitations of the model; its accuracy and the possibility of real time use during invasive investigations. It continues with the discussion of some clinical applications and its didactical value.

Chapter five contains the summary.
In chapter six all equations used to conduct an impulse through a segment are listed.
In chapter seven the equations related to the introduction of impulses into a segment are given.

Samenvatting

Deze studie beschrijft een wiskundig model van het geleidingssysteem van het hart. Met behulp van dit model is het mogelijk tachycardieën op basis van reentry te simuleren. Ook kan men de invloed van extra stimuli en medicatie op deze tachycardieën nagaan. Zo kan de onderzoeker hypotheses toetsen over het mechanisme van tachycardieën, zoals die zijn opgewekt tijdens invasief
electrophysiologisch onderzoek bij patiënten met reentry tachycardieën.
In hoofdstuk een wordt een korte inleiding gegeven over de geschiedenis van het onderzoek naar de oorzaken van ritmestoornissen van het hart. Verder wordt een overzicht gegeven van een aantal in de cardiale electrophysiologie gebruikte simulatiemodellen. Het hoofdstuk wordt afgesloten met een omschrijving van de eisen waaraan het in dit proefschrift omschreven model dient te voldoen.
In hoofdstuk twee volgt een beschrijving van het model. Aan de orde komen de opbouw van het model, een beschrijving van de bouwstenen (segmenten) waaruit het model is samengesteld en een beschouwing betreffende de rol die de segmenten in de voortgeleiding door deze segmenten plaatsvindt. Tevens wordt aangegeven welke impulsen door de segmenten geregeld zijn, alsmede hoe nieuwe impulsen in de segmenten kunnen worden geïntroduceerd. Tenslotte worden de consequenties van een tweetal beperkingen van het model gedemonstreerd.
In hoofdstuk drie worden drie simulaties besproken, te weten de simulatie van het normale geleidingssysteem van het hart, gevolgd door de simulatie van een cirkel tachycardie in een patiënt met het WPW syndroom. In het derde voorbeeld wordt gedemonstreerd hoe een op grond van klinisch onderzoek ontstane hypothese betreffende het aan een tachycardie een feitelijk effect ligt en de rol die de segmenten in de voortgeleiding door deze segmenten plaatsvindt. Tevens wordt aangegeven welke impulsen door de segmenten geregeld zijn, alsmede hoe nieuwe impulsen in de segmenten kunnen worden geïntroduceerd. Tenslotte worden de consequenties van twee beperkingen van het model gedemonstreerd.
In hoofdstuk vier wordt aandacht besteed aan de beperkingen van het model als onderwerp voor een onderzoek. Hoofdstuk vijf bevat de samenstelling van alle vergelijkingen, die geïntroduceerd zijn bij de geleding van een impuls door een segment.
In hoofdstuk zeven worden de vergelijkingen gegeven, die bij het introduceren van een nieuwe impuls in een van de segmenten van het model worden toegepast.

**Rizumee**

Dit beukse eksplikeert un wiskunstig medel vaan ut geleijingssisteem vaan ut hart. Met behöllpe vaan dit medel is ut meugeik um tachycardieen op basis vaan reentry te simuleres. Aoch is ut meuglik de oetwerking vaan vreuger koemende hartsleeg en medikaminte op dees tachycardieen noa ut kieke. Zoe kin den onderzeiker hieptese sjekke euer ut mekaniek vaan tachycardieen, wie die weure opgewek bei inwendig elektrofiesiologies onderzeuk bei lui ut reentrytachycardieen.

In sjapiter een weurd unne korte inleijing gegeeeve euer de gesjiedenis vaan ut onderzeuk noa oerzaake vaan hartkloppinge. Weiier weurd un euerzieg gegeeeve vaan un aanat in de elektrofiesiologie vaan ut hart gebruikde simulasie medelle. Ut sjapiter weurd afgesloete met un besrijving vaan vereiste boeson in dit buuske besjreeve medel mout voldoën. In sjapiter twie steet un besrijving vaan ut medel. Daorin weurd geneump de samestellung vaan ut medel, un besrijving vaan de oonderdeie (segminte) boe
oet ut medel bestuit, en un fielezofie euver de vollegorde boe in de geleijing door dees segminte verlop. Aoch weurd verduws wie de geleijing vaan unnen impuls door zoen segminte geregeid is en wie impulse in de segminte weure ingevoer. Aon ut ind weure de konsekwinsies vaan twie beperrekinge vaan ut medel oetgelag.

In sjapiter dri weure dri simulaasieoonderzejke geexplikeerd, naamlik de simulaasie vaan ut gewone geleijingssisteem vaan ut hart, dan de simulaasie vaan unne sirrekel tachycardie vaan unne mins met de krenkde vaan Wolff, Parkinson en White. In ut derde voorbeeld weurd getuindo wie me unne heipose kin sjekke dee oontstande is nao aonleijing vaan klimes onderzeuk noa ut mekaniek vaan hartkloppinge.

In sjapiter veer weurd aondach geweijt aon de beperrekinge vaan ut medel, wie perseis ut medel werrek en aoch of ut meugelik is beij inwendig onderzeuk ut medel touw te passe. Weijer weure un aontal klimes toejnpassinge geeexplikeerd en aoch of ut medel in ut onderwies gebruik kin weure.

Sjapiter velf bevat dun rizzumee.

Sjapiter zes gief un euverziech vaan alle wiskunstige vergeliekinge die gebruik weure beij de geleijing vaan unnen impuls door un segminte.

In sjapiter zev weurd de vergeliekinge gegeevoe die weure gebruik beij de introduksie vaan unnen neuje impuls in ein vaan de segminte vaan ut medel.
Chapter 6.

Appendix I: Handling of a segment

The following equations summarize the handling of the 35 different states if no external impulses are entered into the segment and conduction velocity and refractory period remain constant.

\[ \text{AP}_n, \text{RP}_n, \text{AL}_n \ldots \] determine the state in the \( n \)th simulation cycle.

\[ \text{AP}_{n+1}, \text{RP}_{n+1}, \text{AL}_{n+1} \ldots \] determine the state in the \((n+1)\)th simulation cycle.

\( \text{ST}_n, \text{ST}_n 2, \text{ST}_n 3 \) etc represent State 1, 2, 3 etc during the \((n)\)th simulation cycle.

\begin{align*}
\text{ST 1:} & \quad \text{AP}_n = 0 \quad \text{RP}_n = 0 \quad \text{AL}_n = 0 \quad \text{RL}_n = 0 \quad \text{AT}_n = 0 \quad \text{RT}_n = 0 \quad \text{CP}_n = 0 \\
& \quad \text{AP}_{n+1} = 0 \quad \text{RP}_{n+1} = 0 \quad \text{AL}_{n+1} = 0 \quad \text{RL}_{n+1} = 0 \quad \text{AT}_{n+1} = 0 \quad \text{RT}_{n+1} = 0 \quad \text{CP}_{n+1} = 0 \\
& \quad \text{ST}_{n+1} = \text{ST} 1
\end{align*}

\begin{align*}
\text{ST 2:} & \quad \text{AP}_n > 0 \quad \text{RP}_n = 0 \quad \text{AL}_n = 0 \quad \text{RL}_n = 0 \quad \text{AT}_n > 0 \quad \text{RT}_n = 0 \quad \text{CP}_n = 0 \\
& \quad \text{RP}_{n+1} = 0 \quad \text{AL}_{n+1} = 0 \quad \text{RL}_{n+1} = 0 \quad \text{RT}_{n+1} = 0 \quad \text{CP}_{n+1} = 0 \\
& \quad \text{AP}_{n+1} = \text{AP}_n + \text{AD} \\
& \quad \text{IF} (\text{AP}_{n+1} \geq 100) \quad \text{THEN:} \quad \text{AP}_{n+1} = 0 \quad \text{ST}_{n+1} = \text{ST} 3 \\
& \quad \text{ELSE:} \quad \text{AP}_{n+1} = \text{AP}_{n+1} \quad \text{ST}_{n+1} = \text{ST} 2 \\
& \quad \text{AT}_{n+1} = \text{AT}_n - 1
\end{align*}

\begin{align*}
\text{ST 3:} & \quad \text{AP}_n = 0 \quad \text{RP}_n = 0 \quad \text{AL}_n = 0 \quad \text{RL}_n = 0 \quad \text{AT}_n > 0 \quad \text{RT}_n = 0 \quad \text{CP}_n = 0 \\
& \quad \text{AP}_{n+1} = 0 \quad \text{RP}_{n+1} = 0 \quad \text{AL}_{n+1} = 0 \quad \text{RL}_{n+1} = 0 \quad \text{RT}_{n+1} = 0 \quad \text{CP}_{n+1} = 0 \\
& \quad \text{AT}_{n+1} = \text{AT}_n - 1 \\
& \quad \text{IF} (\text{AT}_{n+1} = 0) \quad \text{THEN:} \quad \text{AL}_{n+1} = 1 \quad \text{ST}_{n+1} = \text{ST} 4 \\
& \quad \text{ELSE:} \quad \text{AL}_{n+1} = 0 \quad \text{ST}_{n+1} = \text{ST} 3
\end{align*}
ST 4.  $\text{AP}_n=0$ $\text{RP}_n=0$ $\text{AL}_n>0$ $\text{RL}_n=0$ $\text{AT}_n=0$ $\text{RT}_n=0$ $\text{CP}_n=0$

$\text{AP}_{n+1}=0$ $\text{RP}_{n+1}=0$ $\text{AL}_{n+1}=0$ $\text{AT}_{n+1}=0$ $\text{RT}_{n+1}=0$ $\text{CP}_{n+1}=0$

$\text{AL}_{n+1}=\text{AL}_n + \text{AD}$

IF $(\text{AL}_{n+1} \geq 100)$

THEN: $\text{AL}_{n+1}=0$

ELSE: $\text{AL}_{n+1}=\text{AL}_n + \text{1}$

$\text{ST}_{n+1}=\text{ST 1}$

$\text{ST}_{n+1}=\text{ST 4}$

ST 5.  $\text{AP}_n>0$ $\text{RP}_n=0$ $\text{AL}_n>0$ $\text{RL}_n=0$ $\text{AT}_n>0$ $\text{RT}_n=0$ $\text{CP}_n=0$

$\text{RP}_{n+1}=0$ $\text{RL}_{n+1}=0$ $\text{RT}_{n+1}=0$ $\text{CP}_{n+1}=0$

$\text{AP}_{n+1}=\text{AP}_n + \text{AD}$

$\text{AL}_{n+1}=\text{AL}_n + \text{AD}$

IF $(\text{AL}_{n+1} \geq 100)$

THEN: $\text{AL}_{n+1}=0$

ELSE: $\text{AL}_{n+1}=\text{AL}_n + \text{1}$

$\text{ST}_{n+1}=\text{ST 2}$

$\text{ST}_{n+1}=\text{ST 5}$

$\text{AT}_{n+1}=\text{AT}_n - 1$

ST 6.  $\text{AP}_n=0$ $\text{RP}_n>0$ $\text{AL}_n=0$ $\text{RL}_n=0$ $\text{AT}_n=0$ $\text{RT}_n>0$ $\text{CP}_n=0$

$\text{AP}_{n+1}=0$ $\text{AL}_{n+1}=0$ $\text{RL}_{n+1}=0$ $\text{AT}_{n+1}=0$ $\text{CP}_{n+1}=0$

$\text{RP}_{n+1}=\text{RP}_n - \text{RD}$

IF $(\text{RP}_{n+1} \leq 1)$

THEN: $\text{RP}_{n+1}=0$

ELSE: $\text{RP}_{n+1}=\text{RP}_n + 1$

$\text{ST}_{n+1}=\text{ST 7}$

$\text{ST}_{n+1}=\text{ST 6}$

$\text{RT}_{n+1}=\text{RT}_n - 1$

ST 7.  $\text{AP}_n=0$ $\text{RP}_n=0$ $\text{AL}_n=0$ $\text{RL}_n=0$ $\text{AT}_n=0$ $\text{RT}_n>0$ $\text{CP}_n=0$

$\text{AP}_{n+1}=0$ $\text{RP}_{n+1}=0$ $\text{AL}_{n+1}=0$ $\text{AT}_{n+1}=0$ $\text{CP}_{n+1}=0$

$\text{RT}_{n+1}=\text{RT}_n - 1$

IF $(\text{RT}_{n+1}=0)$

THEN: $\text{RL}_{n+1}=100$

ELSE: $\text{RL}_{n+1}=0$

$\text{ST}_{n+1}=\text{ST 8}$

$\text{ST}_{n+1}=\text{ST 7}$
ST 8. \( \text{AP}_n=0 \quad \text{RP}_n=0 \quad \text{AL}_n=0 \quad \text{RL}_n>0 \quad \text{AT}_n=0 \quad \text{RT}_n=0 \quad \text{CP}_n=0 \)

\[
\begin{align*}
\text{AP}_{n+1} &= 0 \\
\text{RP}_{n+1} &= 0 \\
\text{AL}_{n+1} &= 0 \\
\text{AT}_{n+1} &= 0 \\
\text{RT}_{n+1} &= 0 \\
\text{CP}_{n+1} &= 0 \\
\text{RL}_{n+1} &= \text{RL}_n - \text{RD}
\end{align*}
\]

IF (\(\text{RL}_{n+1} \leq 1\))

THEN: \(\text{RL}_{n+1} = 0\)

ELSE: \(\text{ST}_{n+1} = \text{ST} 8\)

ST 9. \( \text{AP}_n=0 \quad \text{RP}_n>0 \quad \text{AL}_n=0 \quad \text{RL}_n>0 \quad \text{AT}_n=0 \quad \text{RT}_n>0 \quad \text{CP}_n=0 \)

\[
\begin{align*}
\text{AP}_{n+1} &= 0 \\
\text{AL}_{n+1} &= 0 \\
\text{AT}_{n+1} &= 0 \\
\text{CP}_{n+1} &= 0 \\
\text{RL}_{n+1} &= \text{RL}_n - \text{RD}
\end{align*}
\]

IF (\(\text{RL}_{n+1} \leq 1\))

THEN: \(\text{RL}_{n+1} = 0\)

ELSE: \(\text{ST}_{n+1} = \text{ST} 9\)

\(\text{RT}_{n+1} = \text{RT}_n - 1\)

ST 10. \( \text{AP}_n>0 \quad \text{RP}_n>0 \quad \text{AL}_n=0 \quad \text{RL}_n=0 \quad \text{AT}_n>0 \quad \text{RT}_n>0 \quad \text{CP}_n=0 \)

\[
\begin{align*}
\text{AL}_{n+1} &= 0 \\
\text{RL}_{n+1} &= 0
\end{align*}
\]

IF \((\text{RP}_n - \text{AP}_n) \leq (\text{AD} + \text{RD}))

THEN: \(\text{AP}_{n+1} = 0\)

ELSE: \(\text{AP}_{n+1} = \text{AP}_{n+1} + \text{AD}\)

\[
\begin{align*}
\text{RP}_{n+1} &= 0 \\
\text{CP}_{n+1} &= \text{AP}_n + \text{AD} * \text{PD} \\
\text{ST}_{n+1} &= \text{ST} 10
\end{align*}
\]

\[
\begin{align*}
\text{AT}_{n+1} &= \text{AT}_n - 1 \\
\text{RT}_{n+1} &= \text{RT}_n - 1
\end{align*}
\]
ST 11. \( AP_n = 0 \) \( RP_n = 0 \) \( AL_n = 0 \) \( RL_n = 0 \) \( AT_n > 0 \) \( RT_n > 0 \) \( CP_n > 0 \)

\[
\begin{align*}
AP_{n+1} &= 0 \quad RP_{n+1} = 0 \quad CP_{n+1} > 0 \\
AT_{n+1} &= AT_n - 1 \\
\text{IF} (AT_{n+1} = 0) \quad \text{THEN}: \quad AL_{n+1} = 1 \\
&\quad \quad \quad \text{ELSE}: \quad AL_{n+1} = 0 \\
&\quad \quad \quad \quad ST_{n+1} = ST_{12} \\
RT_{n+1} &= RT_n - 1 \\
\text{IF} (RT_{n+1} = 0) \quad \text{THEN}: \quad RL_{n+1} = 100 \\
&\quad \quad \quad \text{ELSE}: \quad RL_{n+1} = 0 \\
&\quad \quad \quad \quad ST_{n+1} = ST_{n+1} \\
\text{IF} (ST_{n+1} = ST_{12}) \quad \text{THEN}: \quad ST_{n+1} = ST_{18} \\
&\quad \quad \quad \text{ELSE}: \quad ST_{n+1} = ST_{13}
\end{align*}
\]

ST 12. \( AP_n = 0 \) \( RP_n = 0 \) \( AL_n = 0 \) \( RL_n = 0 \) \( AT_n = 0 \) \( RT_n > 0 \) \( CP_n > 0 \)

\[
\begin{align*}
AP_{n+1} &= 0 \quad RP_{n+1} = 0 \quad AT_{n+1} = 0 \quad CP_{n+1} > 0 \\
AL_{n+1} &= AL_n + AD \\
\text{IF} (AL_{n+1} = CP_n) \quad \text{THEN}: \quad AL_{n+1} = 0 \\
&\quad \quad \quad \text{ELSE}: \quad AL_{n+1} = AL_{n+1} \\
&\quad \quad \quad \quad ST_{n+1} = ST_{14} \\
RT_{n+1} &= RT_n - 1 \\
\text{IF} (RT_{n+1} = 0) \quad \text{THEN}: \quad RL_{n+1} = 100 \\
&\quad \quad \quad \text{ELSE}: \quad RL_{n+1} = 0 \\
&\quad \quad \quad \quad ST_{n+1} = ST_{n+1} \\
\text{IF} (ST_{n+1} = ST_{14}) \quad \text{THEN}: \quad ST_{n+1} = ST_{16} \\
&\quad \quad \quad \text{ELSE}: \quad ST_{n+1} = ST_{18}
\end{align*}
\]
ST 13. \( AP_n = 0 \) \( RP_n = 0 \) \( AL_n = 0 \) \( RL_n = 0 \) \( AT_n = 0 \) \( RT_n = 0 \) \( CP_n = 0 \)

\[ AP_{n+1} = 0 \]
\[ RP_{n+1} = 0 \]
\[ RT_{n+1} = 0 \]
\[ AL_{n+1} = 0 \]
\[ RL_{n+1} = RL_n - RD \]

IF \( RL_{n+1} \leq CP_n \)
THEN \( RL_{n+1} = 0 \)
ELSE \( RL_{n+1} = RL_n + 1 \)
\[ ST_{n+1} = ST_{15} \]
ST \( n+1 = ST_{13} \)

\[ AT_{n+1} = AT_n - 1 \]

IF \( AT_{n+1} = 0 \)
THEN \( AL_{n+1} = 1 \)
ELSE \( AL_{n+1} = 0 \)
\[ ST_{n+1} = ST_{n+1} \]

IF \( ST_{n+1} = ST_{15} \)
THEN \( ST_{n+1} = ST_{17} \)
ELSE \( ST_{n+1} = ST_{18} \)

ST 14. \( AP_n = 0 \) \( RP_n = 0 \) \( AL_n = 0 \) \( RL_n = 0 \) \( AT_n = 0 \) \( RT_n > 0 \) \( CP_n > 0 \)

\[ AP_{n+1} = 0 \]
\[ RP_{n+1} = 0 \]
\[ AL_{n+1} = 0 \]
\[ RL_{n+1} = 0 \]
\[ AT_{n+1} = 0 \]
\[ RT_{n+1} = RT_n - 1 \]

IF \( RT_{n+1} = 0 \)
THEN \( RL_{n+1} = 100 \)
ELSE \( RL_{n+1} = 0 \)
\[ ST_{n+1} = ST_{16} \]
ST \( n+1 = ST_{14} \)

ST 15. \( AP_n = 0 \) \( RP_n = 0 \) \( AL_n = 0 \) \( RL_n > 0 \) \( AT_n = 0 \) \( RT_n = 0 \) \( CP_n > 0 \)

\[ AP_{n+1} = 0 \]
\[ RP_{n+1} = 0 \]
\[ AL_{n+1} = 0 \]
\[ RL_{n+1} = 0 \]
\[ AT_{n+1} = 0 \]
\[ RT_{n+1} = AT_n - 1 \]

IF \( AT_{n+1} = 0 \)
THEN \( AL_{n+1} = 1 \)
ELSE \( AL_{n+1} = 0 \)
\[ ST_{n+1} = ST_{17} \]
ST \( n+1 = ST_{15} \)

ST 16. \( AP_n = 0 \) \( RP_n = 0 \) \( AL_n = 0 \) \( RL_n > 0 \) \( AT_n = 0 \) \( RT_n = 0 \) \( CP_n > 0 \)

\[ AP_{n+1} = 0 \]
\[ RP_{n+1} = 0 \]
\[ AL_{n+1} = 0 \]
\[ RL_{n+1} = 0 \]
\[ RT_{n+1} = 0 \]
\[ CP_{n+1} = 0 \]

IF \( RL_{n+1} \leq CP_n \)
THEN \( RL_{n+1} = 0 \)
ELSE \( RL_{n+1} = 0 \)
\[ ST_{n+1} = ST_{19} \]
ST \( n+1 = ST_{16} \)
ST 17. \( AP_n = 0 \quad RP_n = 0 \quad AL_n > 0 \quad RL_n = 0 \quad AT_n = 0 \quad RT_n = 0 \quad CP_n > 0 \)

\( AP_{n+1} = 0 \quad RP_{n+1} = 0 \quad RL_{n+1} = 0 \quad AT_{n+1} = 0 \quad RT_{n+1} = 0 \quad CP_{n+1} > 0 \)

\( AL_{n+1} = AL_n + AD \)

IF \((AL_{n+1} \geq CP_n)\)
THEN: \( AL_{n+1} = 0 \)
ELSE: \( AL_{n+1} = AL_n + 1 \)
\( ST_{n+1} = ST 19 \)

ST 18. \( AP_n = 0 \quad RP_n = 0 \quad AL_n > 0 \quad RL_n > 0 \quad AT_n = 0 \quad RT_n = 0 \quad CP_n > 0 \)

\( AP_{n+1} = 0 \quad RP_{n+1} = 0 \quad AT_{n+1} = 0 \quad RT_{n+1} = 0 \quad CP_{n+1} > 0 \)

\( AL_{n+1} = AL_n + AD \)

IF \((AL_{n+1} \geq CP_n)\)
THEN: \( AL_{n+1} = 0 \)
ELSE: \( AL_{n+1} = AL_n + 1 \)
\( ST_{n+1} = ST 16 \)

\( RL_{n+1} = RL_n - RD \)

IF \((RL_{n+1} \geq CP_n)\)
THEN: \( RL_{n+1} = 0 \)
ELSE: \( RL_{n+1} = RL_n + 1 \)
\( ST_{n+1} = ST 16 \)

IF \((ST_{n+1} = ST 16)\)
THEN: \( ST_{n+1} = ST 19 \)
ELSE: \( ST_{n+1} = ST 17 \)

ST 19. \( AP_n = 0 \quad RP_n = 0 \quad AL_n = 0 \quad RL_n = 0 \quad AT_n = 0 \quad RT_n = 0 \quad CP_n > 0 \)

\( AP_{n+1} = 0 \quad RT_{n+1} = 0 \quad AL_{n+1} = 0 \quad RL_{n+1} = 0 \quad AT_{n+1} = 0 \quad RT_{n+1} = 0 \quad CP_{n+1} = 0 \)
\( ST_{n+1} = ST 1 \)
ST 26: \( AP_n > 0 \quad RP_n = 0 \quad AL_n > 0 \quad RL_n = 0 \quad AT_n > 0 \quad RT_n > 0 \quad CP_n > 0 \)

\[
\begin{align*}
RP_{n+1} &> 0 \quad CP_{n+1} > 0 \\
AP_{n+1} &> AP_n + AD \\
AL_{n+1} &> AL_n + AD \\
\text{IF (} &AL_{n+1} > CP_n\text{)} \\
\text{THEN:} &\quad AL_{n+1} = 0 \\
\text{ELSE:} &\quad AL_{n+1} = AL_n + 1 \\
ST_{n+1} &> ST 22 \\
\text{ST}_{n+1} &> ST 20 \\
AT_{n+1} &> AT_n - 1 \\
RT_{n+1} &> RT_n - 1 \\
\text{IF (} &RT_{n+1} = 0\text{)} \\
\text{THEN:} &\quad RL_n = 100 \\
\text{ELSE:} &\quad RL_{n+1} = 0 \\
\text{IF (} &ST_{n+1} = ST 22\text{)} \\
\text{THEN:} &\quad ST_{n+1} = ST 25 \\
\text{ELSE:} &\quad ST_{n+1} = ST 28 \\
\end{align*}
\]

ST 21: \( AP_n = 0 \quad RP_n > 0 \quad AL_n = 0 \quad RL_n > 0 \quad AT_n > 0 \quad RT_n > 0 \quad CP_n > 0 \)

\[
\begin{align*}
AP_{n+1} &> 0 \quad CP_{n+1} > 0 \\
RP_{n+1} &> RP_n - RD \\
RL_{n+1} &> RL_n - RD \\
\text{IF (} &RL_{n+1} \leq CP_n\text{)} \\
\text{THEN:} &\quad RL_{n+1} = 0 \\
\text{ELSE:} &\quad RL_{n+1} = RL_n + 1 \\
ST_{n+1} &> ST 23 \\
\text{ST}_{n+1} &> ST 21 \\
AT_{n+1} &> AT_n - 1 \\
\text{IF (} &AT_{n+1} = 0\text{)} \\
\text{THEN:} &\quad AL_{n+1} = 1 \\
\text{ELSE:} &\quad AL_{n+1} = 0 \\
\text{IF (} &ST_{n+1} = ST 23\text{)} \\
\text{THEN:} &\quad ST_{n+1} = ST 27 \\
\text{ELSE:} &\quad ST_{n+1} = ST 29 \\
\end{align*}
\]
ST 22. \(AP_{n+1} > 0\) \(RP_{n+1} = 0\) \(AL_{n+1} = 0\) \(RL_{n} = 0\) \(AT_{n+1} = 0\) \(RT_{n+1} = 0\) \(CP_{n+1} = 0\)

\[\begin{align*}
RP_{n+1} &= 0 \quad AL_{n+1} = 0 \quad CP_{n+1} = 0 \\
AP_{n+1} &= AP_{n} + AD \\
IF (AP_{n+1} = CP_{n}) \quad THEN: \quad AP_{n+1} &= 0 \\
& \quad ELSE: \quad ST_{n+1} = ST_{11} \\
& \quad ST_{n+1} = ST_{22} \\
AT_{n+1} &= AT_{n} - 1 \\
RT_{n+1} &= RT_{n} - 1 \\
IF (RT_{n+1} = 0) \quad THEN: \quad RL_{n+1} = 100 \\
& \quad ELSE: \quad RL_{n+1} = 0 \\
& \quad ST_{n+1} = ST_{n+1} \\
& \quad IF (ST_{n+1} = ST_{11}) \quad THEN: \quad ST_{n+1} = ST_{13} \\
& \quad ELSE: \quad ST_{n+1} = ST_{25}
\end{align*}\]

ST 23. \(AP_{n} = 0\) \(RP_{n} = 0\) \(AL_{n} = 0\) \(RL_{n} = 0\) \(AT_{n} = 0\) \(RT_{n} = 0\) \(CP_{n} > 0\)

\[\begin{align*}
AP_{n+1} &= 0 \quad RL_{n+1} = 0 \quad CP_{n+1} = 0 \\
RP_{n+1} &= RP_{n} - RD \\
IF (RP_{n+1} \leq CP_{n}) \quad THEN: \quad RP_{n+1} &= 0 \\
& \quad ELSE: \quad ST_{n+1} = ST_{11} \\
& \quad ST_{n+1} = ST_{23} \\
AT_{n+1} &= AT_{n} - 1 \\
IF (AT_{n} = 1) \quad THEN: \quad AL_{n+1} = 1 \\
& \quad ELSE: \quad AL_{n+1} = 0 \\
& \quad IF (ST_{n+1} = ST_{11}) \quad THEN: \quad ST_{n+1} = ST_{12} \\
& \quad ELSE: \quad ST_{n+1} = ST_{27} \\
RT_{n+1} &= RT_{n} - 1
\end{align*}\]
ST 24. AP<sub>n</sub> = 0 RP<sub>n</sub> = 0 AL<sub>n</sub> = 0 RL<sub>n</sub> = 0 AT<sub>n</sub> = 0 RT<sub>n</sub> = 0 CP<sub>n</sub> = 0

\[ AP_{n+1} = 0 \quad AL_{n+1} = 0 \quad AT_{n+1} = 0 \quad CP_{n+1} > 0 \]
\[ RP_{n+1} = RP_n - RD \]
\[ RL_{n+1} = RL_n - RD \]

IF (RL<sub>n+1</sub> ≤ CP<sub>n</sub>)
  THEN: RL<sub>n+1</sub> = 0
  ELSE: RL<sub>n+1</sub> = RL<sub>n</sub> + 1
  ST<sub>n+1</sub> = ST 32

\[ RT_{n+1} = RT_n - 1 \]

ST 25. AP<sub>n</sub> > 0 RP<sub>n</sub> = 0 AL<sub>n</sub> = 0 RL<sub>n</sub> = 0 AT<sub>n</sub> = 0 RT<sub>n</sub> = 0 CP<sub>n</sub> = 0

\[ RP_{n+1} = 0 \quad AL_{n+1} = 0 \quad RT_{n+1} = 0 \quad CP_{n+1} > 0 \]
\[ AP_{n+1} = AP_n + AD \]

IF (AP<sub>n+1</sub> ≥ CP<sub>n</sub>)
  THEN: AP<sub>n+1</sub> = 0
  ELSE: AP<sub>n+1</sub> = AP<sub>n</sub> + 1
  ST<sub>n+1</sub> = ST 13

\[ RL_{n+1} = RL_n - RD \]

IF (RL<sub>n+1</sub> ≤ CP<sub>n</sub>)
  THEN: RL<sub>n+1</sub> = 0
  ELSE: RL<sub>n+1</sub> = RL<sub>n</sub> + 1
  ST<sub>n+1</sub> = ST 25

\[ ST_{n+1} = ST 13 \]

\[ AT_{n+1} = AT_n - 1 \]

ST 26. AP<sub>n</sub> > 0 RP<sub>n</sub> = 0 AL<sub>n</sub> = 0 RL<sub>n</sub> = 0 AT<sub>n</sub> = 0 RT<sub>n</sub> = 0 CP<sub>n</sub> = 0

\[ RP_{n+1} = 0 \quad RL_{n+1} = 0 \quad RT_{n+1} = 0 \quad CP_{n+1} > 0 \]
\[ AP_{n+1} = AP_n + AD \]
\[ AL_{n+1} = AL_n + AD \]

IF (AL<sub>n+1</sub> ≥ CP<sub>n</sub>)
  THEN: AL<sub>n+1</sub> = 0
  ELSE: AL<sub>n+1</sub> = AL<sub>n</sub> + 1
  ST<sub>n+1</sub> = ST 31

\[ AT_{n+1} = AT_n - 1 \]
ST 27. \( A_{P_n} = 0 \) \( R_{P_n} > 0 \) \( A_{L_n} > 0 \) \( R_{L_n} = 0 \) \( A_{T_n} = 0 \) \( R_{T_n} > 0 \) \( C_{P_n} > 0 \)

\[ A_{P_n+1} = 0 \]
\[ R_{P_n+1} = 0 \]
\[ A_{T_n+1} = 0 \]
\[ C_{P_n+1} > 0 \]
\[ R_{P_n+1} = R_{P_n} - RD \]

IF \( R_{P_n+1} \leq C_{P_n} \)
THEN: \( R_{P_n+1} = 0 \)
ELSE: \( R_{P_n+1} = R_{P_n} + 1 \)
\[ S_{T_n+1} = ST 12 \]
\[ S_{T_n+1} = ST 27 \]
\[ A_{L_n+1} = A_{L_n} + AD \]

IF \( A_{L_n+1} \geq C_{P_n} \)
THEN: \( A_{L_n+1} = 0 \)
ELSE: \( A_{L_n+1} = A_{L_n} + 1 \)
\[ S_{T_n+1} = S_{T_n+1} \]

IF (\( S_{T_n+1} = ST 12 \))
THEN: \( S_{T_n+1} = ST 14 \)
ELSE: \( S_{T_n+1} = ST 32 \)

\[ R_{T_n+1} = R_{T_n} - 1 \]

ST 28. \( A_{P_n} > 0 \) \( R_{P_n} = 0 \) \( A_{L_n} > 0 \) \( R_{L_n} = 0 \) \( A_{T_n} > 0 \) \( R_{T_n} = 0 \) \( C_{P_n} > 0 \)

\[ R_{P_n+1} = 0 \]
\[ R_{T_n+1} = 0 \]
\[ C_{P_n+1} > 0 \]
\[ A_{P_n+1} = A_{P_n} + AD \]
\[ A_{L_n+1} = A_{L_n} + AD \]

IF \( A_{L_n+1} \geq C_{P_n} \)
THEN: \( A_{L_n+1} = 0 \)
ELSE: \( A_{L_n+1} = A_{L_n} + 1 \)
\[ S_{T_n+1} = ST 25 \]
\[ S_{T_n+1} = ST 29 \]
\[ R_{L_n+1} = R_{L_n} - RD \]

IF \( R_{L_n+1} \leq C_{P_n} \)
THEN: \( R_{L_n+1} = 0 \)
ELSE: \( R_{L_n+1} = R_{L_n} + 1 \)
\[ S_{T_n+1} = S_{T_n+1} \]

IF (\( S_{T_n+1} = ST 25 \))
THEN: \( S_{T_n+1} = ST 31 \)
ELSE: \( S_{T_n+1} = ST 36 \)

\[ A_{T_n+1} = A_{T_n} - 1 \]
ST 29. \( AP_n = 0 \) \( RP_n > 0 \) \( AL_n > 0 \) \( RL_n > 0 \) \( AT_n = 0 \) \( RT_n > 0 \) \( CP_n > 0 \)

\[
\begin{align*}
AP_{n+1} &= 0, \quad AT_{n+1} = 0, \quad CP_{n+1} > 0 \\
RP_{n+1} &= RF_n - RD \\
AL_{n+1} &= AL_n + AD \\
\text{IF} (AL_{n+1} \geq CP_n) \\
&\quad \text{THEN: } AL_{n+1} = 0 \\
&\quad \text{ELSE: } AL_{n+1} = AL_{n+1} \\
&\quad ST_{n+1} = ST 24 \\
&\quad ST_{n+1} = ST 29 \\
RL_{n+1} &= RL_n - RD \\
\text{IF} (RL_{n+1} \leq CP_n) \\
&\quad \text{THEN: } RL_{n+1} = 0 \\
&\quad \text{ELSE: } RL_{n+1} = RL_{n+1} \\
&\quad ST_{n+1} = ST 32 \\
&\quad ST_{n+1} = ST 27 \\
RT_{n+1} &= RT_n - 1
\end{align*}
\]

ST 30. \( AP_n = 0 \) \( RP_n > 0 \) \( AL_n > 0 \) \( RL_n > 0 \) \( AT_n > 0 \) \( RT_n > CP_n > 0 \)

\[
\begin{align*}
CP_{n+1} &= 0 \\
AP_{n+1} &= AP_n + AD \\
RP_{n+1} &= RF_n - RD \\
AL_{n+1} &= AL_n + AD \\
\text{IF} (AL_{n+1} \geq CP_n) \\
&\quad \text{THEN: } AL_{n+1} = 0 \\
&\quad \text{ELSE: } AL_{n+1} = AL_{n+1} \\
&\quad ST_{n+1} = ST 34 \\
&\quad ST_{n+1} = ST 30 \\
RL_{n+1} &= RL_n - RD \\
\text{IF} (RL_{n+1} \leq CP_n) \\
&\quad \text{THEN: } RL_{n+1} = 0 \\
&\quad \text{ELSE: } RL_{n+1} = RL_{n+1} \\
&\quad ST_{n+1} = ST 34 \\
&\quad ST_{n+1} = ST 33 \\
&\quad ST_{n+1} = ST 35 \\
AT_{n+1} &= AT_n - 1 \\
RT_{n+1} &= RT_n - 1
\end{align*}
\]
ST 31. \(AP_n > 0\) \(RP_n = 0\) \(AL_n = 0\) \(RL_n = 0\) \(AT_n > 0\) \(RT_n = 0\) \(CP_n > 0\)

\[RP_{n+1} = 0\]

\[AL_{n+1} = 0\]

\[RL_{n+1} = 0\]

\[RT_{n+1} = 0\]

\[AP_{n+1} = AP_n + AD\]

IF \((AP_{n+1} \geq CP_n)\)

THEN: \(AP_{n+1} = 0\)

ELSE: \(AP_{n+1} = AP_n + 1\)

\[ST_{n+1} = ST 15\]

\[ST_{n+1} = ST 2\]

\[CP_{n+1} = CP_n\]

\[CP_{n+1} = 0\]

\[AT_{n+1} = AT_n - 1\]

ST 32. \(AP_n = 0\) \(RP_n > 0\) \(AL_n = 0\) \(RL_n = 0\) \(AT_n = 0\) \(RT_n > 0\) \(CP_n > 0\)

\[AP_{n+1} = 0\]

\[AL_{n+1} = 0\]

\[RL_{n+1} = 0\]

\[RT_{n+1} = 0\]

\[RP_{n+1} = RP_n - RD\]

IF \((RP_{n+1} \leq CP_n)\)

THEN: \(RP_{n+1} = 0\)

ELSE: \(RP_{n+1} = RP_n + 1\)

\[ST_{n+1} = ST 14\]

\[ST_{n+1} = ST 8\]

\[CP_{n+1} = CP_n\]

\[CP_{n+1} = 0\]

\[RT_{n+1} = RT_n - 1\]

ST 33.

\[AP_n > 0\] \(RP_n = 0\) \(AL_n = 0\) \(RL_n = 0\) \(AT_n > 0\) \(RT_n > 0\) \(CP_n > 0\)

\[AL_{n+1} = 0\]

\[RL_{n+1} = 0\]

\[CP_{n+1} = 0\]

\[AP_{n+1} = AP_n + AD\]

IF \((AP_{n+1} \geq CP_n)\)

THEN: \(AP_{n+1} = 0\)

ELSE: \(AP_{n+1} = AP_n + 1\)

\[ST_{n+1} = ST 23\]

\[ST_{n+1} = ST 33\]

\[RP_{n+1} = RP_n - RD\]

IF \((RP_{n+1} \leq CP_n)\)

THEN: \(RP_{n+1} = 0\)

ELSE: \(RP_{n+1} = RP_n + 1\)

\[ST_{n+1} = ST_{n+1}\]

IF \((ST_{n+1} = ST 23)\)

THEN: \(ST_{n+1} = ST 11\)

ELSE: \(ST_{n+1} = ST 22\)

\[AT_{n+1} = AT_n - 1\]

\[RT_{n+1} = RT_n - 1\]
ST 34. \( A_{Pn} \geq 0 \) \( R_{Pn} \geq 0 \) \( A_{Ln} = 0 \) \( R_{Ln} \geq 0 \) \( A_{Tn} \geq 0 \) \( R_{Tn} \geq 0 \) \( C_{Pn} > 0 \)

\[
\begin{align*}
A_{Ln+1} &= 0 \quad C_{Pn+1} = 0 \\
A_{Pn+1} &= A_{Pn} + A_D \\
\text{IF} \ (A_{Pn+1} \neq C_{Pn}) \\
\quad \text{THEN:} \quad A_{Pn+1} &= 0 \quad ST_{n+1} = ST_{21} \\
& \quad \text{ELSE:} \quad A_{Pn+1} = A_{Pn+1} \quad ST_{n+1} = ST_{34} \\
R_{Pn+1} &= R_{Pn} - RD \\
R_{Ln+1} &= R_{Ln} - RD \\
\text{IF} \ (R_{Ln+1} \leq C_{Pn}) \\
\quad \text{THEN:} \quad R_{Ln+1} &= 0 \\
& \quad \text{ELSE:} \quad R_{Ln+1} = R_{Ln+1} \quad ST_{n+1} = ST_{n+1} \\
& \quad \text{IF} \ (ST_{n+1} = ST_{21}) \\
\quad \text{THEN:} \quad ST_{n+1} = ST_{23} \quad \text{ELSE:} \quad ST_{n+1} = ST_{33} \\
A_{Tn+1} &= A_{Tn} - 1 \\
R_{Tn+1} &= R_{Tn} - 1
\end{align*}
\]

ST 35. \( A_{Pn} \geq 0 \) \( R_{Pn} \geq 0 \) \( A_{Ln} > 0 \) \( R_{Ln} = 0 \) \( A_{Tn} \geq 0 \) \( R_{Tn} > 0 \) \( C_{Pn} > 0 \)

\[
\begin{align*}
R_{Ln+1} &= 0 \quad C_{Pn+1} = 0 \\
A_{Pn+1} &= A_{Pn} + A_D \\
R_{Pn+1} &= R_{Pn} - RD \\
\text{IF} \ (R_{Pn+1} \leq C_{Pn}) \\
\quad \text{THEN:} \quad R_{Pn+1} &= 0 \\
& \quad \text{ELSE:} \quad R_{Pn+1} = R_{Pn+1} \quad ST_{n+1} = ST_{35} \\
A_{Ln+1} &= A_{Ln} + AD \\
\text{IF} \ (A_{Ln+1} \neq C_{Pn}) \\
\quad \text{THEN:} \quad A_{Ln+1} &= 0 \\
& \quad \text{ELSE:} \quad A_{Ln+1} = A_{Ln+1} \quad ST_{n+1} = ST_{n+1} \\
& \quad \text{IF} \ (ST_{n+1} = ST_{20}) \\
\quad \text{THEN:} \quad ST_{n+1} = ST_{22} \quad \text{ELSE:} \quad ST_{n+1} = ST_{33} \\
A_{Tn+1} &= A_{Tn} - 1 \\
R_{Tn+1} &= R_{Tn} - 1
\end{align*}
\]
Chapter 7

Appendix II: The introduction of a new impulse
A DESCRIPTION IN THE 38 DIFFERENT STATES

ST 1. \( A_{P_n} = 0 \), \( R_{P_n} = 0 \), \( A_{L_n} = 0 \), \( R_{L_n} = 0 \), \( A_{T_n} = 0 \), \( R_{T_n} = 0 \), \( C_{P_n} = 0 \)

ANTEROGRade

\[
\begin{align*}
A_{P_{n+1}} &= 1 \\
R_{P_{n+1}} &= 0 \\
A_{L_{n+1}} &= 0 \\
R_{L_{n+1}} &= 0 \\
A_{T_{n+1}} &= 0 \\
R_{T_{n+1}} &= 0 \\
C_{P_{n+1}} &= 0 \\
S_{T_{n+1}} &= S_{T 2}
\end{align*}
\]

RETROGRade

\[
\begin{align*}
A_{P_{n+1}} &= 0 \\
R_{P_{n+1}} &= 100 \\
A_{L_{n+1}} &= 0 \\
R_{L_{n+1}} &= 0 \\
A_{T_{n+1}} &= 0 \\
R_{T_{n+1}} &= 0 \\
C_{P_{n+1}} &= 0 \\
S_{T_{n+1}} &= S_{T 6}
\end{align*}
\]

ST 2. \( A_{P_n} > 0 \), \( R_{P_n} = 0 \), \( A_{L_n} = 0 \), \( R_{L_n} = 0 \), \( A_{T_n} > 0 \), \( R_{T_n} = 0 \), \( C_{P_n} = 0 \)

ANTEROGRade REFRACTORY

\[
\begin{align*}
A_{P_{n+1}} &= 0 \\
R_{P_{n+1}} &= 0 \\
A_{L_{n+1}} &= 0 \\
R_{L_{n+1}} &= 0 \\
A_{T_{n+1}} &= 0 \\
R_{T_{n+1}} &= 0 \\
C_{P_{n+1}} &= 0 \\
S_{T_{n+1}} &= S_{T 10}
\end{align*}
\]

RETROGRade

\[
\begin{align*}
A_{P_{n+1}} &= 0 \\
R_{P_{n+1}} &= 100 \\
A_{L_{n+1}} &= 0 \\
R_{L_{n+1}} &= 0 \\
A_{T_{n+1}} &= 0 \\
R_{T_{n+1}} &= 0 \\
C_{P_{n+1}} &= 0 \\
S_{T_{n+1}} &= S_{T 10}
\end{align*}
\]

ST 3. \( A_{P_n} = 0 \), \( R_{P_n} = 0 \), \( A_{L_n} = 0 \), \( R_{L_n} = 0 \), \( A_{T_n} > 0 \), \( R_{T_n} = 0 \), \( C_{P_n} = 0 \)

ANTEROGRade

\[
\begin{align*}
A_{P_{n+1}} &= 0 \\
R_{P_{n+1}} &= 0 \\
A_{L_{n+1}} &= 0 \\
R_{L_{n+1}} &= 0 \\
A_{T_{n+1}} &= 0 \\
R_{T_{n+1}} &= 0 \\
C_{P_{n+1}} &= 0
\end{align*}
\]

RETROGRade REFRACTORY

\[
\begin{align*}
A_{P_{n+1}} &= 0 \\
R_{P_{n+1}} &= 0 \\
A_{L_{n+1}} &= 0 \\
R_{L_{n+1}} &= 0 \\
A_{T_{n+1}} &= 0 \\
R_{T_{n+1}} &= 0 \\
C_{P_{n+1}} &= 0
\end{align*}
\]
ST 4. $AP_n=0$ $RP_n=0$ $AL_n>0$ $RL_n=0$ $AT_n=0$ $RT_n=0$ $CP_n=0$

ANTEROGRADE

$RP_{n+1}=0$ $AL_{n+1}>0$ $RL_{n+1}=0$ $AT_{n+1}=0$ $RT_{n+1}=0$ $CP_{n+1}=0$

IF ($AL_{n+1}>(1+AD))$

THEN : $AP_{n+1}=1$

ELSE : $AP_{n+1}=0$

$AT_{n+1}=ARP$

$ST_{n+1}=ST 5$

$ST_{n+1}=ST 4$

RETOGRADE REFRACATORY

$AP_{n+1}=0$ $RP_{n+1}=0$ $AL_{n+1}>0$ $RL_{n+1}=0$ $AT_{n+1}=0$ $RT_{n+1}=0$ $CP_{n+1}=0$

ST 5. $AP_n>0$ $RP_n=0$ $AL_n>0$ $RL_n=0$ $AT_n>0$ $RT_n=0$ $CP_n=0$

ANTEROGRADE REFRACATORY

$AP_{n+1}>=0$ $RP_{n+1}=0$ $AL_{n+1}>=0$ $RL_{n+1}=0$ $AT_{n+1}=0$ $RT_{n+1}=0$ $CP_{n+1}=0$

RETOGRADE REFRACATORY

$AP_{n+1}>=0$ $RP_{n+1}=0$ $AL_{n+1}>=0$ $RL_{n+1}=0$ $AT_{n+1}=0$ $RT_{n+1}=0$ $CP_{n+1}=0$

ST 6. $AP_n=0$ $RP_n>0$ $AL_n=0$ $RL_n=0$ $AT_n=0$ $RT_n>0$ $CP_n=0$

ANTEROGRADE

$AP_{n+1}=1$ $RP_{n+1}>=0$ $AL_{n+1}>=0$ $RL_{n+1}=0$ $AT_{n+1}=ARP$ $RT_{n+1}>=0$ $CP_{n+1}=0$

$ST_{n+1}=ST 10$

RETOGRADE REFRACATORY

$AP_{n+1}=0$ $RP_{n+1}=0$ $AL_{n+1}=0$ $RL_{n+1}=0$ $AT_{n+1}=0$ $RT_{n+1}>0$ $CP_{n+1}=0$

ST 7. $AP_n=0$ $RP_n=0$ $AL_n=0$ $RL_n=0$ $AT_n=0$ $RT_n>0$ $CP_n=0$

ANTEROGRADE REFRACATORY

$AP_{n+1}=0$ $RP_{n+1}=0$ $AL_{n+1}=0$ $RL_{n+1}=0$ $AT_{n+1}=0$ $RT_{n+1}>0$ $CP_{n+1}=0$

RETOGRADE REFRACATORY

$AP_{n+1}=0$ $RP_{n+1}=0$ $AL_{n+1}=0$ $RL_{n+1}=0$ $AT_{n+1}=0$ $RT_{n+1}>0$ $CP_{n+1}=0$
ST 8. \( AP_n = 0 \) \( RP_n = 0 \) \( AL_n = 0 \) \( RL_n > 0 \) \( AT_n = 0 \) \( RT_n = 0 \) \( CP_n = 0 \)

ANTEROGRADE REFRACTORY

\( AP_{n+1} = 0 \) \( RP_{n+1} = 0 \) \( AL_{n+1} = 0 \) \( RL_{n+1} > 0 \) \( AT_{n+1} = 0 \) \( RT_{n+1} = 0 \) \( CP_{n+1} = 0 \)

RETROGRADE

\( AP_{n+1} = 0 \) \( AL_{n+1} = 0 \) \( RL_{n+1} > 0 \) \( AT_{n+1} = 0 \) \( CP_{n+1} = 0 \)

IF \( (RL_{n+1} < (100 - RD)) \)
THEN: \( RP_{n+1} = 100 \) ELSE: \( RP_{n+1} = 0 \)
\( RT_{n+1} = RRP \) \( ST_{n+1} = ST 8 \)

ST 9. \( AP_n = 0 \) \( RP_n > 0 \) \( AL_n = 0 \) \( RL_n > 0 \) \( AT_n = 0 \) \( RT_n > 0 \) \( CP_n = 0 \)

ANTEROGRADE REFRACTORY

\( AP_{n+1} = 0 \) \( RP_{n+1} > 0 \) \( AL_{n+1} = 0 \) \( RL_{n+1} > 0 \) \( AT_{n+1} = 0 \) \( RT_{n+1} > 0 \) \( CP_{n+1} = 0 \)

RETROGRADE REFRACTORY

\( AP_{n+1} = 0 \) \( RP_{n+1} > 0 \) \( AL_{n+1} = 0 \) \( RL_{n+1} > 0 \) \( AT_{n+1} = 0 \) \( RT_{n+1} > 0 \) \( CP_{n+1} = 0 \)

ST 10. \( AP_n > 0 \) \( RP_n > 0 \) \( AL_n = 0 \) \( RL_n > 0 \) \( AT_n > 0 \) \( RT_n > 0 \) \( CP_n = 0 \)

ANTEROGRADE REFRACTORY

\( AP_{n+1} > 0 \) \( RP_{n+1} > 0 \) \( AL_{n+1} = 0 \) \( RL_{n+1} = 0 \) \( AT_{n+1} > 0 \) \( RT_{n+1} > 0 \) \( CP_{n+1} = 0 \)

RETROGRADE REFRACTORY

\( AP_{n+1} > 0 \) \( RP_{n+1} > 0 \) \( AL_{n+1} = 0 \) \( RL_{n+1} = 0 \) \( AT_{n+1} > 0 \) \( RT_{n+1} > 0 \) \( CP_{n+1} = 0 \)

ST 11. \( AP_n = 0 \) \( RP_n = 0 \) \( AL_n = 0 \) \( RL_n = 0 \) \( AT_n > 0 \) \( RT_n > 0 \) \( CP_n > 0 \)

ANTEROGRADE REFRACTORY

\( AP_{n+1} = 0 \) \( RP_{n+1} = 0 \) \( AL_{n+1} = 0 \) \( RL_{n+1} = 0 \) \( AT_{n+1} > 0 \) \( RT_{n+1} > 0 \) \( CP_{n+1} > 0 \)

RETROGRADE REFRACTORY

\( AP_{n+1} = 0 \) \( RP_{n+1} = 0 \) \( AL_{n+1} = 0 \) \( RL_{n+1} = 0 \) \( AT_{n+1} > 0 \) \( RT_{n+1} > 0 \) \( CP_{n+1} > 0 \)
ST 12. $AP_n=0 \; RP_n=0 \; AL_{n+1}>0 \; RL_{n+1}=0 \; AT_n=0 \; RT_{n+1}>0 \; CP_{n+1}>0$

**ANTEROGRADE**

$RP_{n+1}=0 \; AL_{n+1}>0 \; RL_{n+1}=0 \; RT_{n+1}>0 \; CP_{n+1}>0$

IF $(AL_{n+1}>(1+AD))$

THEN: $AP_{n+1}=1$

ELSE: $AP_{n+1}=0$

$AT_{n+1}=ARP$

$ST_{n+1}=ST\; 20$

$ST_{n+1}=ST\; 12$

**RETROGRADE REFRACTORY**

$AP_{n+1}=0 \; RP_{n+1}=0 \; AL_{n+1}>0 \; RL_{n+1}=0 \; AT_{n+1}=0 \; RT_{n+1}>0 \; CP_{n+1}>0$

ST 13. $AP_n=0 \; RP_n=0 \; AL_n=0 \; RL_n>0 \; AT_n=0 \; RT_n=0 \; CP_n>0$

**ANTEROGRADE REFRACTORY**

$AP_{n+1}=0 \; RP_{n+1}=0 \; AL_{n+1}=0 \; RL_{n+1}>0 \; AT_{n+1}>0 \; RT_{n+1}=0 \; CP_{n+1}>0$

**RETROGRADE**

$AP_{n+1}=0 \; AL_{n+1}=0 \; RL_{n+1}>0 \; AT_{n+1}>0 \; CP_{n+1}>0$

IF $(RL_{n+1}<(1.00-\; RD))$

THEN: $RP_{n+1}=100$

ELSE: $RP_{n+1}=0$

$RT_{n+1}=RBP$

$ST_{n+1}=ST\; 21$

$ST_{n+1}=ST\; 13$

ST 14. $AP_n=0 \; RP_n=0 \; AL_n=0 \; RL_n=0 \; AT_n=0 \; RT_n>0 \; CP_n>0$

**ANTEROGRADE**

$AP_{n+1}=1 \; RP_{n+1}=0 \; AL_{n+1}=0 \; RL_{n+1}=0 \; AT_{n+1}=ARP \; RT_{n+1}>0 \; CP_{n+1}>0$

$ST_{n+1}=ST\; 22$

**RETROGRADE REFRACTORY**

$AP_{n+1}=0 \; RP_{n+1}=0 \; AL_{n+1}=0 \; RL_{n+1}=0 \; AT_{n+1}=0 \; RT_{n+1}>0 \; CP_{n+1}>0$
ST 15. \( AP_n = 0 \) \( RP_n = 0 \) \( AL_n = 0 \) \( RL_n = 0 \) \( AT_n > 0 \) \( RT_n = 0 \) \( CP_n > 0 \)

**ANTEROGRADE REFRACTORY**

\( AP_{n+1} = 0 \) \( RP_{n+1} = 0 \) \( AL_{n+1} = 0 \) \( RL_{n+1} = 0 \) \( AT_{n+1} > 0 \) \( RT_{n+1} = 0 \) \( CP_{n+1} > 0 \)

**RETOGRADE**

\( AP_{n+1} = 0 \) \( RP_{n+1} = 0 \) \( AL_{n+1} = 0 \) \( RL_{n+1} = 100 \) \( AT_{n+1} > 0 \) \( RT_{n+1} = 0 \) \( CP_{n+1} > 0 \)

\( ST_{n+1} = ST 23 \)

ST 16. \( AP_n = 0 \) \( RP_n = 0 \) \( AL_n = 0 \) \( RL_n > 0 \) \( AT_n = 0 \) \( RT_n = 0 \) \( CP_n > 0 \)

**ANTEROGRADE**

\( AP_{n+1} = 1 \) \( RP_{n+1} = 0 \) \( AL_{n+1} = 0 \) \( RL_{n+1} > 0 \) \( AT_{n+1} = ARP \) \( RT_{n+1} = 0 \) \( CP_{n+1} > 0 \)

\( ST_{n+1} = ST 25 \)

**RETOGRADE**

\( AP_{n+1} = 0 \) \( AL_{n+1} = 0 \) \( RL_{n+1} > 0 \) \( AT_{n+1} = 0 \) \( CP_{n+1} > 0 \)

IF \((RL_{n+1} < (100 - RD))\)

THEN: \( RP_{n+1} = 100 \) ELSE: \( RP_{n+1} = 0 \)

\( RT_{n+1} = RRP \) \( RT_{n+1} = 0 \)

\( ST_{n+1} = ST 24 \) \( ST_{n+1} = ST 16 \)

ST 17. \( AP_n = 0 \) \( RP_n = 0 \) \( AL_n > 0 \) \( RL_n = 0 \) \( AT_n = 0 \) \( RT_n = 0 \) \( CP_n > 0 \)

**ANTEROGRADE**

\( RP_{n+1} = 0 \) \( AL_{n+1} > 0 \) \( RL_{n+1} = 0 \) \( RT_{n+1} = 0 \) \( CP_{n+1} > 0 \)

IF \((AL_{n+1} > (1 + AD))\)

THEN: \( AP_{n+1} = 1 \) ELSE: \( AP_{n+1} = 0 \)

\( AT_{n+1} = ARP \) \( AT_{n+1} = 0 \)

\( ST_{n+1} = ST 26 \) \( ST_{n+1} = ST 17 \)

**RETOGRADE**

\( AP_{n+1} = 0 \) \( RP_{n+1} = 100 \) \( AL_{n+1} > 0 \) \( RL_{n+1} = 0 \) \( AT_{n+1} = 0 \) \( RT_{n+1} = RRP \) \( CP_{n+1} > 0 \)

\( ST_{n+1} = ST 27 \)
ST 18. AP_{n+1} = 0 RP_{n+1} = 0 AL_{n+1} > 0 RL_{n+1} > 0 AT_{n+1} = 0 RT_{n+1} = 0 CP_{n+1} > 0

ANTEROGRADE

RP_{n+1} = 0 AL_{n+1} > 0 RL_{n+1} > 0 RT_{n+1} = 0 CP_{n+1} > 0

IF (AL_{n+1} > (I+AD))
THEN: AP_{n+1} = I
ELSE: AP_{n+1} = 0
AT_{n+1} = ARP
ST_{n+1} = ST 28

RETROGRADE

AP_{n+1} = 0 AL_{n+1} > 0 RL_{n+1} > 0 AT_{n+1} = 0 RT_{n+1} = 0 CP_{n+1} > 0

IF (RL_{n+1} < (100-RD))
THEN: RP_{n+1} = 100
ELSE: RP_{n+1} = 0
RT_{n+1} = RRP
ST_{n+1} = ST 59

ST 19. AP_{n+1} = 0 RP_{n+1} = 0 AL_{n+1} = 0 RL_{n+1} = 0 AT_{n+1} = 0 RT_{n+1} = 0 CP_{n+1} > 0

ANTEROGRADE

AP_{n+1} = 1 RP_{n+1} = 0 AL_{n+1} = 0 RL_{n+1} = 0 AT_{n+1} = 0 RT_{n+1} = 0 CP_{n+1} > 0
ST_{n+1} = ST 31

RETROGRADE

AP_{n+1} = 0 RP_{n+1} = 100 AL_{n+1} = 0 RL_{n+1} = 0 AT_{n+1} = 0 RT_{n+1} = 0 CP_{n+1} > 0
ST_{n+1} = ST 32

ST 20. AP_{n+1} = 0 RP_{n+1} = 0 AL_{n+1} = 0 RL_{n+1} = 0 AT_{n+1} = 0 RT_{n+1} = 0 CP_{n+1} > 0

ANTEROGRADE REFRACTORY

AP_{n+1} = 0 RP_{n+1} = 0 AL_{n+1} = 0 RL_{n+1} = 0 AT_{n+1} = 0 RT_{n+1} = 0 CP_{n+1} > 0

RETROGRADE REFRACTORY

AP_{n+1} = 0 RP_{n+1} = 0 AL_{n+1} = 0 RL_{n+1} = 0 AT_{n+1} = 0 RT_{n+1} = 0 CP_{n+1} > 0
ST 21. $A_P = 0 \ R_P > 0 \ A_L = 0 \ R_L > 0 \ A_T > 0 \ R_T > 0 \ C_P > 0$

ANTEROGRADE REFRACTORY

$A_{P+1} = 0 \ R_{P+1} > 0 \ A_{L+1} = 0 \ R_{L+1} > 0 \ A_{T+1} > 0 \ R_{T+1} > 0 \ C_{P+1} > 0$

RETROGRADE REFRACTORY

$A_{P+1} = 0 \ R_{P+1} > 0 \ A_{L+1} = 0 \ R_{L+1} > 0 \ A_{T+1} > 0 \ R_{T+1} > 0 \ C_{P+1} > 0$

ST 22. $A_P > 0 \ R_P = 0 \ A_L = 0 \ R_L > 0 \ A_T > 0 \ R_T > 0 \ C_P > 0$

ANTEROGRADE REFRACTORY

$A_{P+1} > 0 \ R_{P+1} = 0 \ A_{L+1} = 0 \ R_{L+1} = 0 \ A_{T+1} > 0 \ R_{T+1} > 0 \ C_{P+1} > 0$

RETROGRADE REFRACTORY

$A_{P+1} > 0 \ R_{P+1} = 0 \ A_{L+1} = 0 \ R_{L+1} = 0 \ A_{T+1} > 0 \ R_{T+1} > 0 \ C_{P+1} > 0$

ST 23. $A_P = 0 \ R_P > 0 \ A_L = 0 \ R_L = 0 \ A_T > 0 \ R_T > 0 \ C_P > 0$

ANTEROGRADE REFRACTORY

$A_{P+1} = 0 \ R_{P+1} > 0 \ A_{L+1} = 0 \ R_{L+1} = 0 \ A_{T+1} > 0 \ R_{T+1} > 0 \ C_{P+1} > 0$

RETROGRADE REFRACTORY

$A_{P+1} = 0 \ R_{P+1} > 0 \ A_{L+1} = 0 \ R_{L+1} = 0 \ A_{T+1} > 0 \ R_{T+1} > 0 \ C_{P+1} > 0$

ST 24. $A_P = 0 \ R_P > 0 \ A_L = 0 \ R_L > 0 \ A_T = 0 \ R_T > 0 \ C_P > 0$

ANTEROGRADE

$A_{P+1} = 0 \ R_{P+1} = 0 \ A_{L+1} = 0 \ R_{L+1} > 0 \ A_{T+1} = \text{ARP} \ R_{T+1} > 0 \ C_{P+1} > 0$

ST_{n+1} = ST 34

RETROGRADE REFRACTORY

$A_{P+1} = 0 \ R_{P+1} > 0 \ A_{L+1} = 0 \ R_{L+1} > 0 \ A_{T+1} = 0 \ R_{T+1} > 0 \ C_{P+1} > 0$
ST 25  AP_{n+1} > 0  RP_{n+1} = 0  AL_{n+1} = 0  RL_{n+1} > 0  AT_{n+1} > 0  RT_{n+1} = 0  CP_{n+1} > 0

ANTEROGRADELY REFRACTORY

AP_{n+1} > 0  RP_{n+1} = 0  AL_{n+1} = 0  RL_{n+1} > 0  AT_{n+1} > 0  RT_{n+1} = 0  CP_{n+1} > 0

RETROGRADE

AP_{n+1} > 0  AL_{n+1} = 0  RL_{n+1} > 0  RT_{n+1} > 0  CP_{n+1} > 0

IF (RL_{n+1} < (100 - RD))
THEN:  RP_{n+1} = 100  RT_{n+1} = RRP  ST_{n+1} = ST 34
ELSE:  RP_{n+1} = 0  RT_{n+1} = 0  ST_{n+1} = ST 25

ST 26  AP_{n+1} > 0  RP_{n+1} = 0  AL_{n+1} = 0  RL_{n+1} > 0  AT_{n+1} > 0  RT_{n+1} = 0  CP_{n+1} > 0

ANTEROGRADE REFRACTORY

AP_{n+1} > 0  RP_{n+1} = 0  AL_{n+1} = 0  RL_{n+1} > 0  AT_{n+1} > 0  RT_{n+1} = 0  CP_{n+1} > 0

RETROGRADE

AP_{n+1} > 0  RP_{n+1} = 100  AL_{n+1} = 0  RL_{n+1} > 0  AT_{n+1} > 0  RT_{n+1} = RRP  CP_{n+1} > 0  ST_{n+1} = ST 35

ST 27  AP_{n+1} = 0  RP_{n+1} > 0  AL_{n+1} = 0  RL_{n+1} = 0  AT_{n+1} = 0  RT_{n+1} > 0  CP_{n+1} > 0

ANTEROGRADE

RP_{n+1} > 0  AL_{n+1} > 0  RL_{n+1} = 0  RT_{n+1} > 0  CP_{n+1} > 0

IF (AL_{n+1} > (1 + AD))
THEN:  AP_{n+1} = 1  AT_{n+1} = ARP  ST_{n+1} = ST 35
ELSE:  AP_{n+1} = 0  AT_{n+1} = 0  ST_{n+1} = ST 27

RETROGRADE REFRACTORY

AP_{n+1} = 0  RP_{n+1} > 0  AL_{n+1} > 0  RL_{n+1} = 0  AT_{n+1} = 0  RT_{n+1} > 0  CP_{n+1} > 0
ST 28. AP_n>0 RP_n=0 AL_n>0 RL_n>0 AT_n>0 RT_n=0 CP_n>0

ANTEROGRADE REFRACTORY

AP_{n+1}>0 RP_{n+1}=0 AL_{n+1}>0 RL_{n+1}>0 AT_{n+1}>0 RT_{n+1}=0 CP_{n+1}>0

RETROGRADE

AP_{n+1}>0 AL_{n+1}>0 RL_{n+1}>0 AT_{n+1}>0 CP_{n+1}>0

IF (RL_{n+1}<(100-RD))
    THEN: RP_{n+1}=100    ELSE: RP_{n+1}=0
    RT_{n+1}=RRP          RT_{n+1}=0
    ST_{n+1}=ST 30        ST_{n+1}=ST 28

ST 29. AP_n=0 RP_n>0 AL_n>0 RL_n>0 AT_n=0 RT_n>0 CP_n>0

ANTEROGRADE

RP_{n+1}>0 AL_{n+1}>0 RL_{n+1}>0 RT_{n+1}=0 CP_{n+1}>0

IF (AL_{n+1}>(1+AD))
    THEN: AP_{n+1}=1    ELSE: AP_{n+1}=0
    AT_{n+1}=ARP        AT_{n+1}=0
    ST_{n+1}=ST 30      ST_{n+1}=ST 29

RETROGRADELY REFRACTORY

AP_{n+1}=0 RP_{n+1}>0 AL_{n+1}>0 RL_{n+1}>0 AT_{n+1}=0 RT_{n+1}>0 CP_{n+1}>0

ST 30. AP_n>0 RP_n>0 AL_n>0 RL_n>0 AT_n>0 RT_n>0 CP_n>0

ANTEROGRADE REFRACTORY

AP_{n+1}>0 RP_{n+1}>0 AL_{n+1}>0 RL_{n+1}>0 AT_{n+1}>0 RT_{n+1}>0 CP_{n+1}>0

RETROGRADE REFRACTORY

AP_{n+1}>0 RP_{n+1}>0 AL_{n+1}>0 RL_{n+1}>0 AT_{n+1}>0 RT_{n+1}>0 CP_{n+1}>0
ST 31. $AP_{n+1} > 0$, $RP_{n+1} = 0$, $AL_{n+1} = 0$, $RT_{n+1} = 0$, $CP_{n+1} > 0$

ANTEROGRADE REFRACTORY

$AP_{n+1} > 0$, $RP_{n+1} = 0$, $AL_{n+1} = 0$, $RT_{n+1} = 0$, $CP_{n+1} > 0$

Retrograde

$AP_{n+1} > 0$, $RP_{n+1} = 100$, $AL_{n+1} = 0$, $RT_{n+1} = 0$, $CP_{n+1} > 0$

$ST_{n+1} = ST_{33}$

ST 32. $AP_{n} = 0$, $RP_{n} > 0$, $AL_{n} = 0$, $RT_{n} = 0$, $CP_{n} > 0$

ANTEROGRADE

$AP_{n+1} = 1$, $RP_{n+1} > 0$, $AL_{n+1} = 0$, $RT_{n+1} = 0$, $CP_{n+1} > 0$

$ST_{n+1} = ST_{33}$

RETROGRADE REFRACTORY

$AP_{n+1} = 0$, $RP_{n+1} > 0$, $AL_{n+1} = 0$, $RT_{n+1} = 0$, $CP_{n+1} > 0$

ST 33. $AP_{n} > 0$, $RP_{n} > 0$, $AL_{n} = 0$, $RT_{n} = 0$, $CP_{n} > 0$

ANTEROGRADE REFRACTORY

$AP_{n+1} > 0$, $RP_{n+1} > 0$, $AL_{n+1} = 0$, $RT_{n+1} > 0$, $CP_{n+1} > 0$

RETROGRADE REFRACTORY

$AP_{n+1} > 0$, $RP_{n+1} > 0$, $AL_{n+1} = 0$, $RT_{n+1} > 0$, $CP_{n+1} > 0$

ST 34. $AP_{n} > 0$, $RP_{n} > 0$, $AL_{n} = 0$, $RT_{n} = 0$, $CP_{n} > 0$

ANTEROGRADE REFRACTORY

$AP_{n+1} > 0$, $RP_{n+1} > 0$, $AL_{n+1} > 0$, $RT_{n+1} > 0$, $CP_{n+1} > 0$

RETROGRADE REFRACTORY

$AP_{n+1} > 0$, $RP_{n+1} > 0$, $AL_{n+1} > 0$, $RT_{n+1} > 0$, $CP_{n+1} > 0$
ST 35. \( A_{P_n} > 0 \) \( R_{P_n} > 0 \) \( A_{L_n} > 0 \) \( R_{L_n} = 0 \) \( A_{T_n} > 0 \) \( R_{T_n} > 0 \) \( C_{P_n} > 0 \)

ANTEROGRADE REFRACTORY

\( A_{P_{n+1}} > 0 \) \( R_{P_{n+1}} > 0 \) \( A_{L_{n+1}} > 0 \) \( R_{L_{n+1}} = 0 \) \( A_{T_{n+1}} > 0 \) \( R_{T_{n+1}} > 0 \) \( C_{P_{n+1}} > 0 \)

RETROGRADE REFRACTORY

\( A_{P_{n+1}} > 0 \) \( R_{P_{n+1}} > 0 \) \( A_{L_{n+1}} > 0 \) \( R_{L_{n+1}} = 0 \) \( A_{T_{n+1}} > 0 \) \( R_{T_{n+1}} > 0 \) \( C_{P_{n+1}} > 0 \)
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Slotwoord

Het werken met simulatiemodellen in de cardiologie is een fascinerende bezigheid. Drie factoren maken de Capaciteitsgroep Cardiologie tot een unieke plaats om aan het onderzoek in de electrophysiologie mee te werken.

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Curriculum vitae
