Gen. Physiol. Biophys. (1983), **2**, 163—167

A Mathematical Model of Afterdepolarizations

I. TIPĀNS and E. LAVENDELS

Riga Polytechnical Institute, Lenin str. 1, 226355 Riga, Latvian SSR, USSR

Abstract. Conditions for the occurrence of delayed afterdepolarizations were analyzed in a mathematical model of the action potential in atrial and ventricular conduction system cells. First, the influence of the rapid repolarization component of the potassium current, the slow inward (calcium) and the sodium backward currents respectively upon the main parameters of afterdepolarizations was examined. In the second series of computation experiments also the other two potassium current components were included. The estimation of ionic currents was carried out in order to determine the oscillation zones of transmembrane potential.

Key words: Mathematical models — Action potential — Afterdepolarizations — Heart muscle — Oscillations

Introduction

When developing mathematical models of action potentials in atrial and ventricular conduction system cells we noted (Lavendels et al. 1981) that at certain values of ionic current conductances after the ordinary action potential, the depolarization and repolarization processes are followed by another depolarization. In some cases this depolarization reached the threshold and another action potential occurred. It was also noted that, at some values of ionic current conductances, not one but a train of oscillations of transmembrane potential occurred in cells which normally do not show automaticity. According to Cranefield (1977) these delayed afterdepolarizations may cause tachycardias, characterized by accelerated rhythm and transition of sites of pacemaker activity. The aim of this work was to determine the influence of ionic current conduction upon the main parameters of afterdepolarization, the maximum level and duration, diastolic potential as well as to estimate the range of conduction in which these afterdepolarizations occur.

Methods

We started with the model of atrial and ventricular cells, developed by Lavendels et al. (1981) and derived from the model (McAllister et al. 1975) of Purkinje fibres membrane action potential in which only the values of ionic currents were varied; terminology and all other values of kinetic variables,

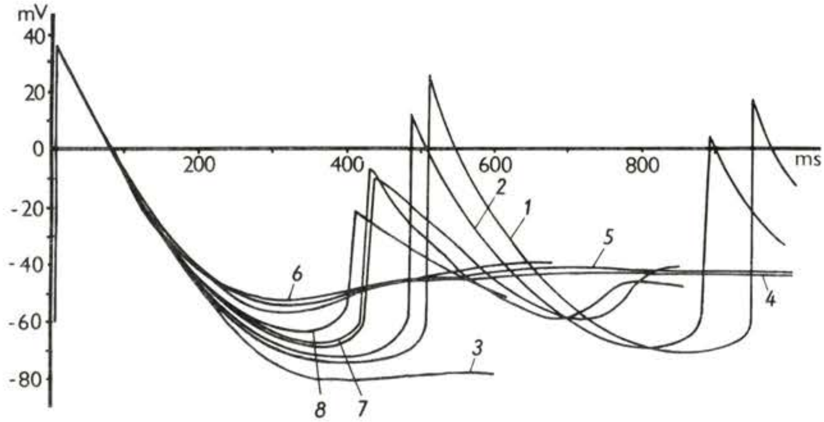

Fig. 1. Transmembrane potential oscillations at different values of coefficients k_{si}, k_{x1}, $k_{Na,b}$.

reversal potentials etc. remained the same as in the model of McAllister et al. (1975). To denote the variations of currents, i_j, the coefficient k_j, was used,

$$i'_j = k_j \cdot i_j ,$$

where i'_j is current which was varied.
The values of ionic currents and transmembrane potential were calculated by solving the 10-th order system of nonlinear differential equations described by McAllister et al. (1975) using the Runge-Kutta's procedure with variable integration step. For the calculation an EC-1050 computer was used, and the total computation time of one action potential was about 15 minutes.

Results and Discussion

First of all, only some currents — slow inward i_{si}, sodium backward $i_{Na,b}$ and the fast component of potassium repolarization current i_{x1} — were varied with $k_{si} = 0.5$; the values of k_{x1} and $k_{Na,b}$ are shown in Table 1, and the corresponding changes of transmembrane potential as the function of time are presented in Fig. 1. It should be noted that in all cases the shape of the action potential remained the same during the first 200 ms. With $k_{si} = 0.5$ and $k_{x1} = 3$ the afterdepolarizations occurred when $k_{Na,b} \in (0.55; 0.8)$. It is to be noticed that an increase in $k_{Na,b}$ changes the value of the resting potential from -80 mV to -45 mV. It was experimentally shown (Morton and Arnsdorf 1977) that there are two stable values of resting potential and that it is possible to induce transition from one value to another by the action of procainamide on Purkinje fibres. Within a narrow range of $k_{Na,b} \in (0.55; 0.7)$ several transmembrane potential oscillations are generated instead of one afterdepolarization. The highest amplitude was observed at $k_{Na,b} = 0.6$. With the increase of $k_{Na,b}$ the frequency of oscillations increased, but their amplitude decreased.

Table 1. Coefficients of variations of ionic currents

No	1	2	3	4	5	6	7	8
k_{x1}	3	3	3	2.7	3	3.3	3.3	3.1
$k_{Na,b}$	0.6	0.62	0.55	0.7	0.8	0.9	0.7	0.7

When $k_{Na,b}$ was further increased, the oscillations ceased and only one afterdepolarization was observed, again, followed by a low resting potential of -50 mV. Finally, at $k_{Na,b}=0.8$, no afterdepolarization could be induced. If in the existence area of afterdepolarizations the potassium current component i_{x1} was increased ($k_{x1}=3.1$ and $k_{x1}=3.3$), the amplitude of the action potential following afterdepolarization was increased. When i_{x1} and $i_{Na,b}$ were increased simultaneously ($k_{x1}=3.3$; $k_{Na,b}=0.9$) the afterdepolarizations were absent and a low level of resting potential was reached. It should be noted that an action potential of the same shape as in the previous case exists when $k_{x1}=2.7$ and $k_{Na,b}=0.7$.

Therefore a more general question arises concerning the possibility of the existence of afterdepolarizations at other sets of values of ionic currents.

To answer this question, two series of computation experiments were performed. First, 20 experiments with k_{si}, k_{x1}, $k_{Na,b}$ varied as follows

$$k_{si} \in (0.4\,;\, 0.6)\,;$$
$$k_{x1} \in (2.8\,;\, 3.2)\,;$$
$$k_{Na,b} \in (0.5\,;\, 0.7),$$

i.e. in the zone certainly including the oscillations and in another, which was wider, where

$$k_{si} \in (0\,;\, 1)$$
$$k_{x1} \in (2\,;\, 4)$$
$$k_{x2} \in (1\,;\, 2)$$
$$k_{K1} \in (0\,;\, 2)$$
$$k_{Na,b} \in (0\,;\, 2)$$

consisting of 40 experiments where two other potassium current components — k_{K1} and k_{x2} were also changed.

In the first series of experiments afterdepolarizations were always encountered. A common feature of all of them was that each cycle of depolarization was characterized by an increased frequency and a decreased amplitude. The correspondance of repolarization and depolarization levels is also remarkable, with

Table 2. The relation between the main parameters of the action potential and coefficients of the ionic currents k_{si}, k_{x1}, k_{x2}, k_{k1}, $k_{Na,b}$

No	k_{si}	k_{x1}	k_{x2}	k_{k1}	$k_{Na,b}$	E_{dp}	E_{ds}	t_o	t_{ds}
						mv		ms	
1	0.125	2.3	1.8	0.35	1.05	36	−40	105	250
2	0.1	3.25	1.625	0.85	1.95	34	−29	70	275
3	0.55	3.05	1.575	2.0	1.8	29	−34	63	350
4	0.175	4.0	1.375	1.350	1.0	27	−49	40	225
5	0.6	3.3	1.975	0.55	1.6	38	−47	120	475
6	0.45	2.75	1.125	0.05	1.2	44	−28	140	250
7	0.05	2.15	1.425	1.25	0.8	27	−51	30	275
8	0.5	2.05	1.15	0.75	1.3	36	−31	115	450
9	0.525	3.9	1.275	0.5	1.65	38	−33	120	340
10	1.0	2.8	1.45	1.7	0.5	33	−92	85	350
11	0.775	3.1	2.0	1.15	0.45	34	−87	85	350
12	0.9	3.2	1.875	0.6	1.25	41	−63	125	850
13	0.025	3.35	1.325	1.9	0.65	24	−87	25	275
14	0.3	2.85	1.075	1.05	0.95	32	−44	65	305
15	0.275	3.65	1.95	0.65	0.55	34	−66	75	"oscillations"
16	0.475	3.7	1.5	0.3	0.05	39	−93	100	325
17	0.975	3.15	1.475	1.3	1.4	36	−35	105	365
18	0.225	3.5	1.025	1.45	1.5	31	−43	50	335
19	0.425	3.4	1.2	1.5	0.15	31	−100	50	225
20	0.075	2.6	1.35	1.75	1.7	24	−41	30	385
21	0.7	3.75	1.675	0.2	0.3	45	−82	113	"oscillations"
22	0.15	2.7	1.525	0.4	1.75	37	−28	115	525
23	0.575	3.6	1.05	0.95	0.75	34	−65	85	"oscillations"
24	0.75	2.55	1.1	1.6	0.35	32	−97	80	365
25	0.95	3.45	1.225	0.15	1.15	50	−29	150	340
26	0.85	2.45	1.725	0.7	1.1	39	−32	120	405
27	0.925	3.85	1.55	0.8	0.7	39	−73	105	"oscillations"
28	0.325	2.5	1.85	1.4	0.2	29	−99	45	280
29	0.2	2.65	1.925	1.2	1.35	31	−40	55	360
30	0.825	2.1	1.9	1.8	0.9	30	−73	80	"oscillations"
31	0.675	2.25	1.4	1.0	0.4	35	−86	95	355
32	0.65	2.2	1.75	1.95	1.9	28	−34	75	335
33	0.35	2.95	1.775	0.9	0.6	34	−64	74	"oscillations"
34	0.625	2.9	1.175	1.55	2.00	31	−32	85	370
35	0.8	2.35	1.25	0.45	1.45	44	−26	150	465
36	0.4	2.4	1.3	0.25	0.25	40	−77	120	"oscillations"
37	0.875	3.0	1.6	1.65	0.1	32	−102	75	285
38	0.25	3.95	1.7	1.1	1.55	31	−40	60	330
39	0.725	3.8	1.65	0.1	1.85	47	−22	140	380
40	0.375	3.55	1.825	0	0.85	44	−36	115	280

t_o — time of reaching the zero level of transmembrane potential, E_{ds} — resting potential, E_{dp} — maximal depolarization level, t_{ds} — approximate duration of the action potential.

higher depolarization spike occurring when the repolarization reached more negative values. In order to exceed the zero level of transmembrane potential the preceding maximum repolarization level should be less negative than -70 mV. If this condition was not satisfied the following depolarization levels were still negative and the steady state value of transmembrane potential was of about -45 mV. The results of the second series of experiments are presented in Table 2. Oscillations of transmembrane potential were observed in seven experiments. It is significant that they occurred at the set of values of k_{si}, k_{x1} and $k_{Na,b}$ which differ considerably from those in the previous series of experiments, where oscillations always existed. It is therefore supposed that the zone of oscillations is not as narrow as expected before or that there exist more than one such zone.

The existence of similarly shaped action potentials at different values of ionic currents means that in some cases the same electric properties of cell membranes may be achieved by distinct action of different pharmacologic agents.

References

Lavendels E. E., Matschabeli L. I., Tipāns I. O. (1981): Construction of a model on the spread of excitation in the conducting system of the heart. In: Theory and Applications of Automatization of the Electrocardiological Clinical Research (Ed. Z. Yanushkevichus), pp. 252—254, Kaunas (in Russian)

Cranefield P. J. (1977): Action potentials, afterpotentials and arhythmias. Circ. Res. **41,** 415—423

Mc Allister R. E., Noble D., Tsien R. W. (1975): Reconstruction of the electrical activity of cardiac Purkinje fibres. J. Physiol. (London) **251,** 1—59

Morton J., Arnsdorf (1977): The effect of antiarhythmic drugs on triggered sustained rhythmic activity in cardiac Purkinje fibres. J. Pharmacol. Exp. Ther. **201,** 689—700

Received August 23, 1982 / Accepted December 6, 1982