MACMAN

A Simulation of Heart, Peripheral Circulation and Arterial Baroreceptor Function

MacMan provides a foundation to understanding the behaviour of the system formed by the brain, heart and circulatory system. Students may easily learn the anatomy of the circulation and the way blood passes around it, but *MacMan* can show them how the system works as an integrated whole, something which many never properly understand. Why does jugular venous pressure go up in cardiogenic shock, and down in haemorrhagic shock? Why is it that positive pressure ventilation causes such profound circulatory disturbances? Why does noradrenaline reduce blood volume and slow down the heart? These are examples of problems that students using *MacMan* will come to understand.

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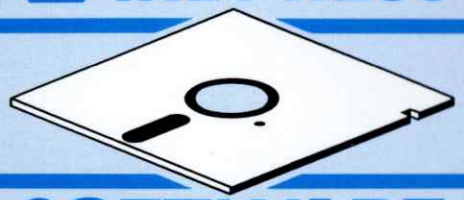

SOFTWARE

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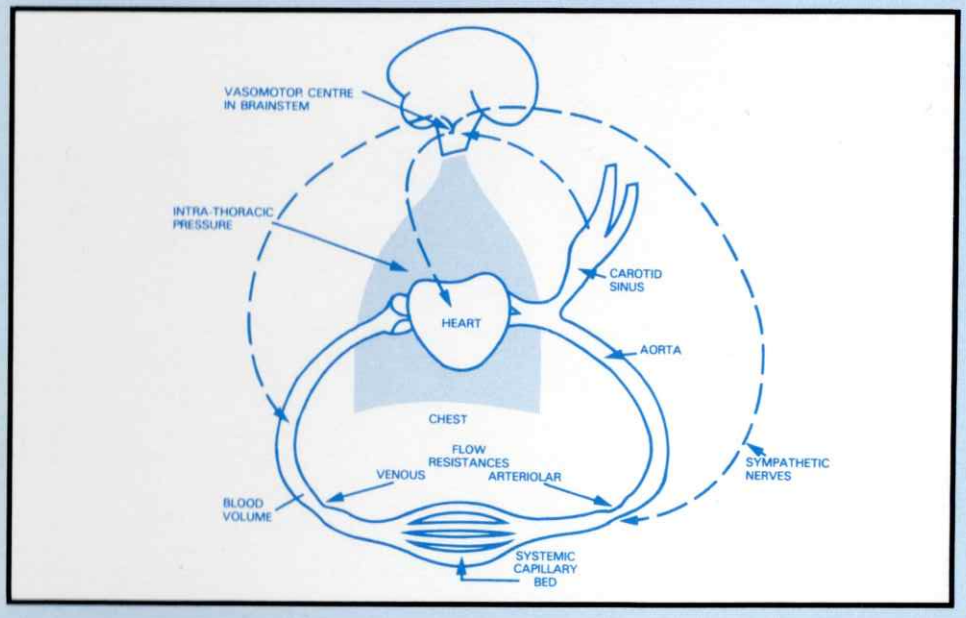

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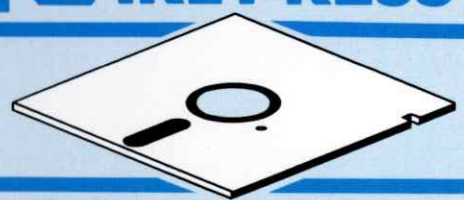

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LIMITATION OF LIABILITY

Mathematical models cannot be expected to provide completely accurate descriptions of the systems under consideration; our aim is to make these models relevant and helpful to someone learning about the behaviour of the system. To this end, they have been revised and developed through many versions over a seventeen-year period and have been in continuous use at many centres during that time.

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1. The model

1.1 Introduction to *MacMan*

MacMan was the first interactive digital computer simulation program in the Mac Series developed at St Bartholomew's Medical College and McMaster University. It represents the behaviour of the structures shown in the diagram (Figure 1). The system looks (and is) very simple. Why bother to have a model for study?

Briefly the answer is that generations of students have learnt the anatomy of the circulation and the way in which the blood passes round it, but have never properly understood how it works as an integrated whole. *MacMan* can help to give you a feeling for the quantitative and integrative aspects. It will make you appreciate, for example, why the jugular venous pressure goes up in cardiogenic shock and down in haemorrhagic shock, why positive pressure ventilation can cause such profound circulatory disturbances, why increased cardiac output can only occur with the co-operation of the systemic vasculature, and why noradrenaline (norepinephrine) should reduce blood volume, and slow down the heart.

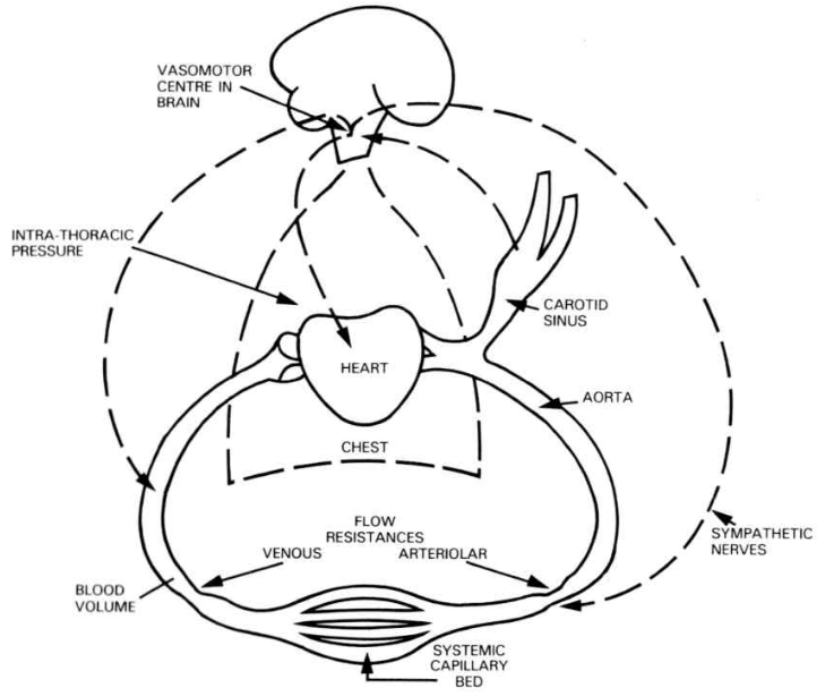


Figure 1. Block diagram of the model.

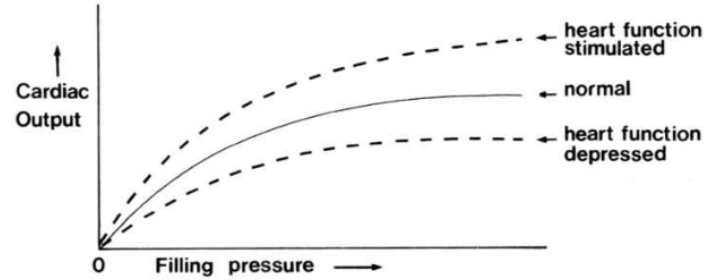


Figure 2. The cardiac function curve.

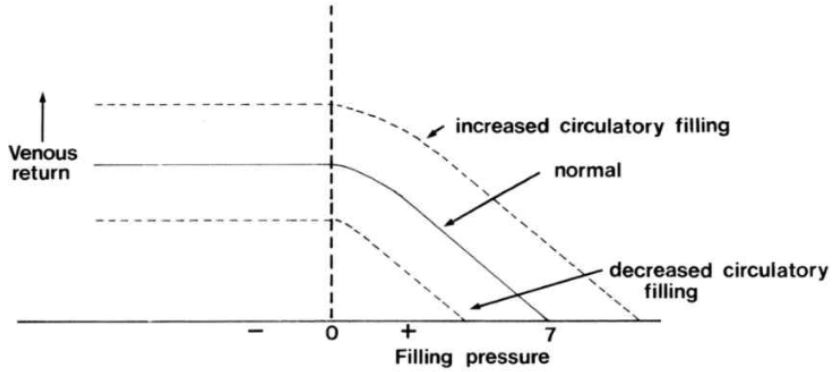


Figure 3. The venous return curve (filling pressure in mm Hg).

1.2 Brief technical description

The structure of the model is as follows.

The heart is considered simply as a pump which has the characteristics described by Starling at the beginning of this century, i.e. an output dependent upon its filling pressure, up to a certain maximum.

The rate of beating of the heart is under central nervous system control through the vagus nerves (slowing it down) and the sympathetic nerves (speeding it up). The sympathetic system, aided by adrenaline from the adrenal medulla, also increases the force of cardiac contraction. Thus the 'Starling curve' for cardiac output as shown in Figure 2 is changeable.

The effective filling pressure is the difference between actual 'central venous pressure' (i.e. right atrial pressure) and the intrathoracic pressure (normally a few mm Hg negative with respect to atmospheric pressure). However, even a very negative pressure inside the chest cannot suck blood out of the venous system, because the veins have thin walls and collapse (Figure 3).

Venous return (the return of blood to the heart) depends on the difference

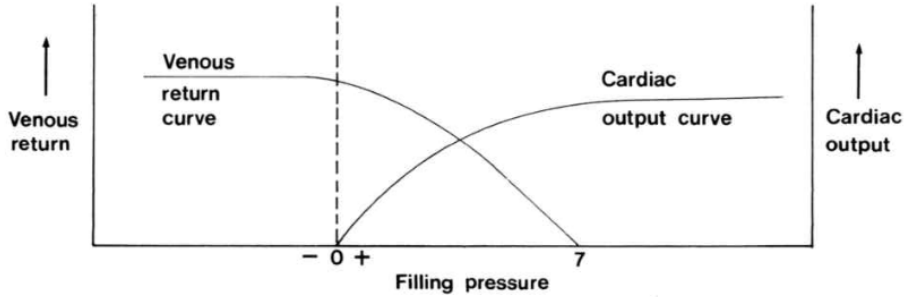


Figure 4. Graphical method for determining the steady state of the system. MacMan performs the same manoeuvre automatically and finds the steady state of the circulation as illustrated. You can check on this in the model, for example, by increasing cardiac function to 1000% of normal (10 times) but you will find that you can only obtain a small extra increase of actual cardiac output.

between the average pressure filling the circulation (mean systemic pressure – about 7 mm Hg above atmospheric) and the right atrial pressure. As for cardiac output, the venous return curve may be altered by anything which changes mean systemic pressure (i.e. altered blood volume or altered circulatory capacitance).

Actual cardiac output has to take account of both cardiac pumping ability and of venous return. Guyton showed that the actual cardiac output (and the actual filling pressure) in any given situation was given by the point of intersection of the two curves (see Figure 4).

The peripheral circulation is represented simply by a lumped arterial resistance and a smaller venous resistance (shown as constricted segments in the circuit diagram). The capillary bed is sandwiched between arteries and veins, and its pressure will obviously be influenced by various things, chiefly the ratio between the values of the two resistances. Most of the blood is contained on the venous side of the circulation, which has a certain capacitance, characterising the pressure/volume relationship.

The autonomic nervous system obtains information about the systemic arterial blood pressure from the carotid sinus baroreceptors and other pressure sensors, and exerts control over heart rate and force of contraction. It also controls arterial resistance and venous capacitance, as indicated in Figure 1.

The blood volume is normally about 5 litres and fills the systemic circulation to give a static pressure of 7 mm Hg (if the heart were to be stopped and all pressures made equal). To improve its clinical realism, *MacMan* has been equipped with appropriate symptoms, signs and nursing reports, and 'death' results if any one of the many variables which are continuously examined passes outside the range compatible with life. In the event of death, *post mortem* reports are issued; after 'death' has occurred, a new subject is automatically created with normal initial values.

1.3 Limitations – conceptual and procedural

The conceptual limitations of *MacMan* reside in its excessive simplicity. The peripheral circulation, for example, cannot be treated under all circumstances as a single compartment with certain values for arterial and venous resistance, and capacitance. It obviously has many compartments. *MacMan* cannot, for example, simulate the apparently paradoxical increase of cardiac output which can occur on clamping the upper abdominal aorta, a manoeuvre which increases arterial resistance but, at the same time, augments venous return by allowing some of the blood in the splanchnic bed to drain into the rest of the circuit. The heart's performance is often limited in disease by selective failure of the left ventricle, leading to an excessive pressure and increased blood volume in the lungs. This cannot be simulated by *MacMan*. The behaviour of the autonomic system is grossly oversimplified (e.g. increased left atrial pressure can accelerate the heart – the 'Bainbridge reflex') and is also not taken account of by *MacMan*.

Procedural limitations are largely those of unfamiliarity, sometimes with the computer keyboard rather than with the computer as such. Don't think of *MacMan* as a computer model, but rather as an incredibly obliging person who will allow all sorts of (sometimes fatal) experiments to be performed on him. Care has been taken to design a model that is easy to use by a novice, and students in many countries to which *MacMan* has been transplanted have had no difficulty. But you still have to learn to use the model, or persuade someone else to show you how. Inevitably, since it works through a computer, there will be some feeling of strangeness, but be assured that no knowledge of computers is needed. If you have any suggestions for improvements in the interactive dialogue for doing experiments with *MacMan*, let us know so that they can be considered.

After familiarizing yourself with *MacMan* through Section 2, you will start to be aware of apparent limitations of speed and convenience. If you then return to this handbook and read Section 3 (for experienced users), you will find that *MacMan* has additional resources available, e.g. the facility to change type of display, to print selected values, and to avoid repetitive interactive dialogue. Section 4 contains some suggested physiological and clinical experiments which you should try to examine. When you can confidently predict the answers to all the suggested experiments you will have mastered the elementary physiology of the systemic circulation, and can extend your experience by using the more complete models, such as *MacPee* and *MacPuf*.

1.4 Implementation

MacMan is written in Fortran 77. It is a restructured and extended version of the original *MacMan* program but the physiological design remains the same.

2. Operating the program – beginners' guide

2.1 How to get started

The program may be run by booting the computer in the usual way, then placing the disk in drive A: and typing 'man' and then ENTER from the DOS 'A>' prompt. Two title pages will be displayed, each of which will clear after a key is pressed.

A text file called 'read.me' included on the disk gives more information about the operation of the software and lists any updates to the manual. Please read this file (for example by typing 'type read.me' from the DOS prompt) before using *MacMan*.

If any menu is unclear, press Q and then ENTER to obtain an explanatory message. To return to the main menu of options from elsewhere in the program, type '*' and press ENTER.

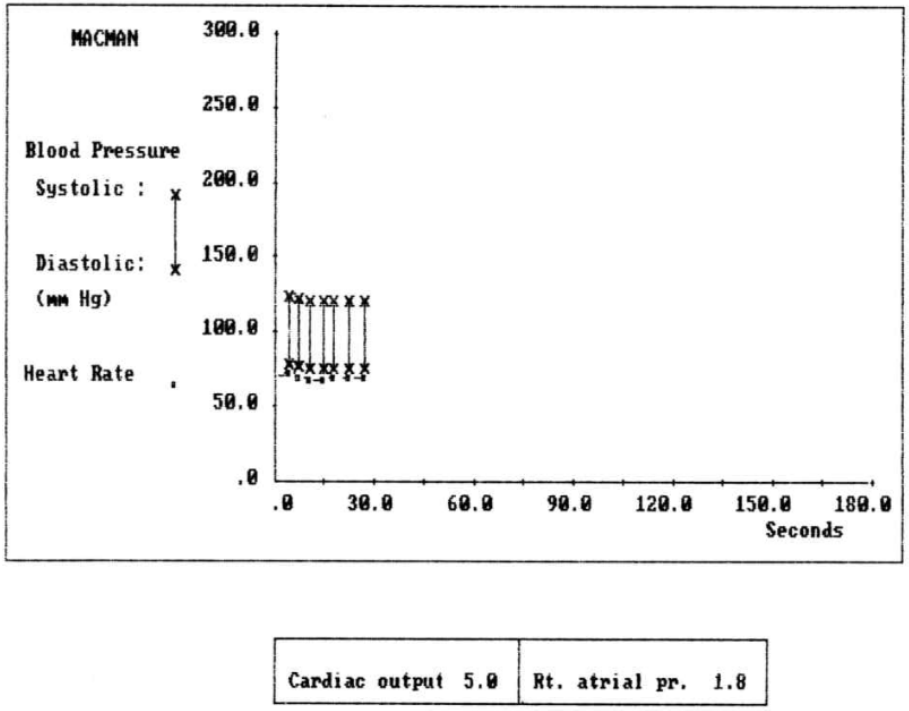
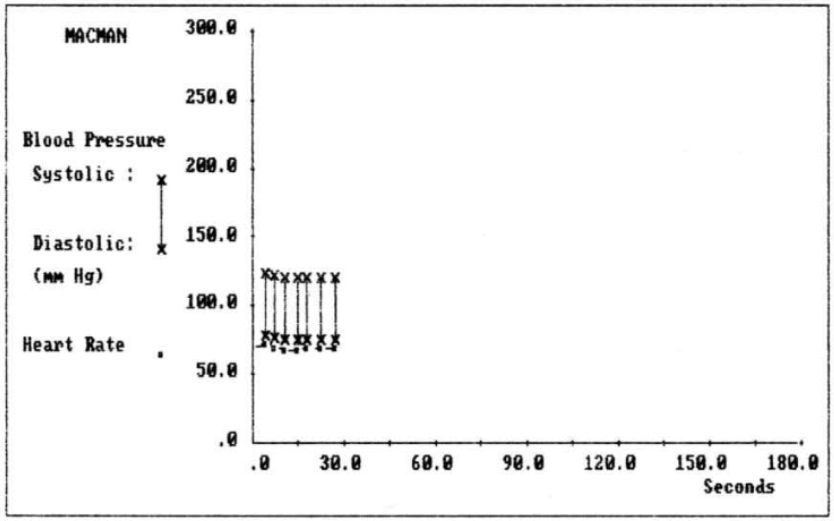


Figure 5. Baseline display of blood pressure and heart rate.




```
B.P. Systolic  =120  mmHg   Right atrial press.=  1.8 mm Hg
     Diastolic = 74         Mean capill.press. = 12.7 mm Hg
     Mean      = 89.9       Cardiac output     =  5.0 l/min
Heart rate     = 70.        Stroke volume      = 71.2 ml
Arterial resistance   =  16.0 mm Hg/l/min
Venous resistance     =   2.2
Cardiac contractility =   1.3 l/min/mm Hg filling press.
```

Figure 6. Baseline measurements obtained from the model.

2.2 Example of an actual run

Figure 5 shows the graph of the standard subject produced automatically on starting up the program. This is a chart of blood pressure (X---X running between systolic and diastolic pressures shown in mm Hg, 1 kPa = 13.3 mm Hg) and heart rate (□) at 4-second time intervals. The time scale (x axis) is in seconds. In the two boxes are displayed current values of cardiac output (in litres/min) and right atrial pressure (in mm Hg).

At the end of the run of calculations, the current values of most of the clinically important values are displayed (Figure 6). Some of these can easily be measured (e.g. blood pressure and heart rate); some are more difficult (e.g. cardiac output); and some are in practice impossible to measure clinically (e.g. mean capillary pressure) but are nonetheless important. You will see that all values are about normal for an average adult male.

The main menu of options for the user is displayed at this point:

```
Do you want to 1. Change,  2. Continue,  3. Restart,  4. Stop
```


Select '2. Continue' and another run lasting one minute will then be displayed. Since nothing has been changed, the values at the end of the run are substantially the same as at the start.

2.3 How to change a factor

Selecting 1 from the main menu of options leads to a section of the program dealing with altering various aspects of the model itself or the output from it. The submenu displayed is:

```
1. Change Factors,  2. Baroreceptor Function,  3. Displays
```

Type the number of factor or factors you want to change; there are six changeable factors as follows:

1. Systemic arterial resistance
2. Systemic venous resistance
3. Cardiac pump performance

(1–3: as a percentage of the normal value for an average adult at rest.)

4. Mean intrathoracic pressure (normally a few mm Hg negative)
5. Blood volume (normally 5000 ml)
6. Venous capacitance (% of normal value)

In the example shown in Figure 7, arterial resistance (factor 1) has been doubled. The sequence of instructions for this example is:

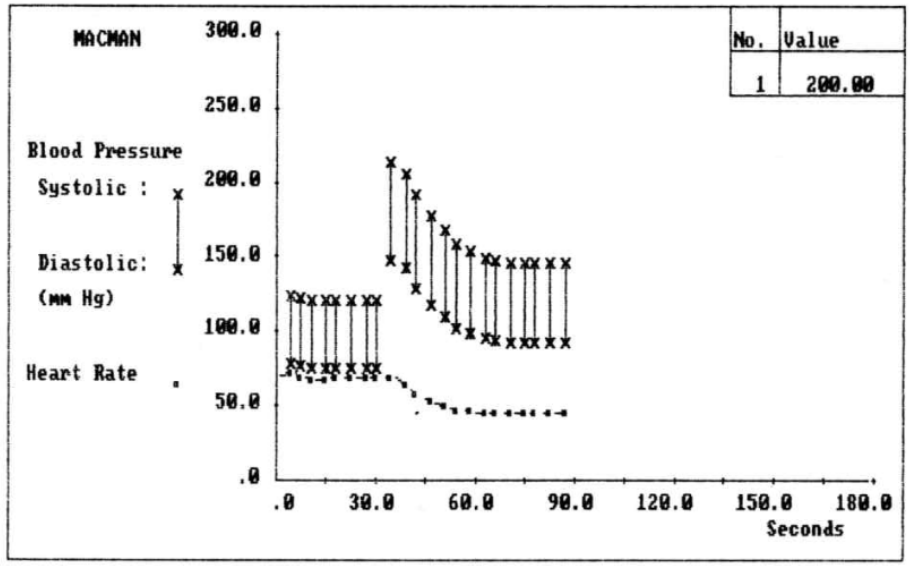
```
Do you want to 1. Change,  2. Continue,  3. Restart,  4. Stop
1
1. Change Factors,  2. Baroreceptor Function,  3. Displays
1
Type the numbers of factors (1-6) to be changed
1
Factor 1 (currently = 100.0), specify new value
200
1. Change,  2. Continue,  3. Restart,  4. Stop
2
```

Note: 1. The acute rise in blood pressure and rapid fall back towards normal as the stabilizing mechanisms start to act.
2. The reflex fall in heart rate, which is also part of the normal response.

The changes are similar to those seen in man or in the dog after infusing noradrenaline at a high rate.

2.4 Suggested preliminary experiments

Take the first three changeable factors and observe the effect of doubling and of halving the value of each. Try making intrathoracic pressure (factor 4) +2 instead of −2 mm Hg and try making blood volume (factor 5) 7000 and 3000 ml. Repeat the same manoeuvres after cutting the buffer nerves (see 3.1 below). Study all the results and make sure you can interpret them. Look especially carefully at capillary pressure and at cardiac output, remembering



B.P. Systolic =145 mmHg Right atrial press.= 2.2 mm Hg
Diastolic = 91 Mean capill.press. = 10.3 mm Hg
Mean =109.4 Cardiac output = 3.7 l/min
Heart rate = 46. Stroke volume = 80.2 ml

Figure 7. Simulation of acute rise in systemic arterial resistance.

that a rise in capillary pressure will tend to make fluid leave the circulation and enter the interstitial space.

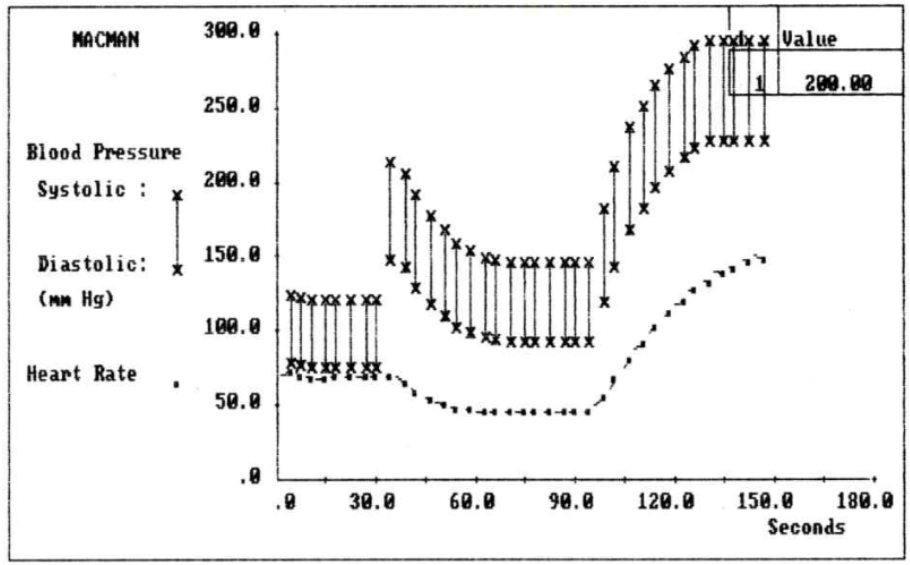
3. How to operate the program – further details

3.1 How to change the baroreceptor function

By selecting option 2 in the change submenu, the user may choose:

1) to cut the buffer nerves;
2) to reset baroreceptor function to that expected of a moderately hypertensive subject.

The example (Figure 8) follows on from the example in Section 2.3. In this case arterial resistance had been doubled, but the baroreceptor reflex had compensated for the change. Cutting the buffer nerves (from the aortic and carotid baroreceptors) removes this control, resulting in a huge rise of blood pressure and heart rate. Death (probably in such a case from brain haemorrhage) would then ensue. On death, current values are printed and a new (intact) subject is automatically created.



I can hardly breathe at all
I feel really terrible
I have a splitting headache

Do you want to 1.Change, 2.Continue, 3.Restart, 4.Stop

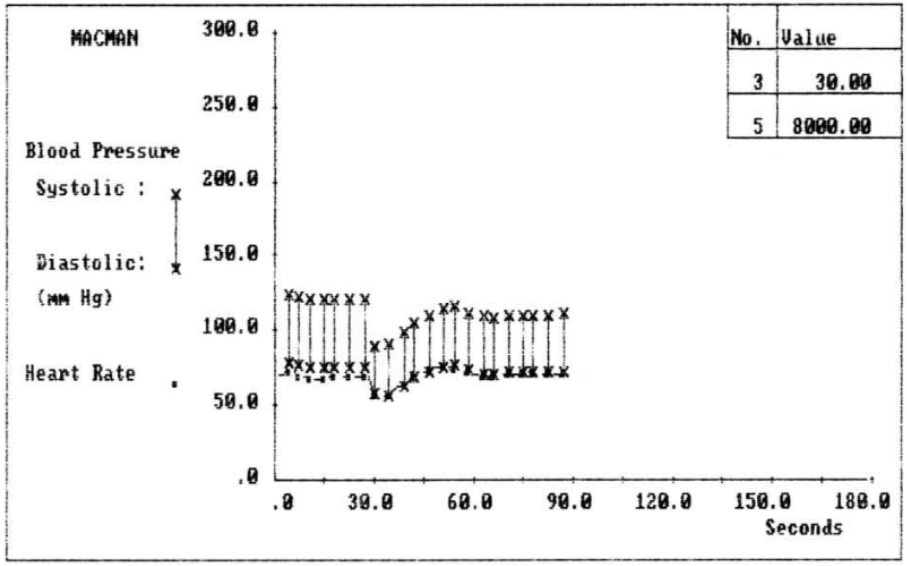
Figure 8. Effect of cutting the buffer nerves on a subject with raised arterial resistance.

Another option available, offered should you decide not to cut the buffer nerves, is to reset the baroreceptor function to that expected of a moderately hypertensive subject.

3.2 Changing more than one factor at once

Since a run does not start until you ask for '2. Continue' from the main menu of options, you can always ask for '1. Change' a second time and change further values until you are ready to continue. However, *MacMan* will accept a string of factor numbers as long as they are separated by spaces. In the example of Figure 9 the user wished to simulate diminished myocardial function (factor 3) and increased blood volume (factor 5), as might be seen in heart failure. Note the appearance, when appropriate, of symptoms.

When you are very familiar with the interactive dialogue, it becomes tedious to wait for the computer to type its next bit of text. Therefore, if you know what is coming, you can enter several responses in one line, separated by



B.P. Systolic	=109 mmHg	Right atrial press.	= 11.9 mm Hg		
Diastolic	= 70	Mean capill.press.	= 20.3 mm Hg		
Mean	= 83.6	Cardiac output	= 3.8 l/min		
Heart rate	= 72.	Stroke volume	= 53.2 ml		

Figure 9. Changing cardiac pump performance and blood volume simultaneously. Note that a large number of experiments can be done quickly and efficiently, so long as you know what you are doing! The display can be changed back to standard form at any time by using this option again.

slashes ('/'), and when all the responses are entered, press the ENTER key. The succeeding questions will be suppressed and the next instruction will be executed in order by the computer without interruption.

As an example the user might ask for

Change (1), Change Factors (1) 3 and 5 to 30 and 7500

This could all be entered with the command

1/1/3 5/30/7500/2

(note separating blank between 3 and 5), and the computer finally instructed to Continue (2).

3.3 Changing the type of display and output of selected values

Select option '1. Change' in the main menu of options, then from the change submenu:

1. Change Factors, 2. Baroreceptor Function, 3. Displays

Time (sec)	Syst.	Diast. Pressure (mm Hg)	Mean	Heart Rate (/min)	Cardiac Output (l/min)	Cardiac Contractility (l/min/mm Hg)	Arterial Resistance (mm Hg/l/min)
96	109	70	83.7	72.	3.8	.5	17.2
102	109	70	83.6	71.	3.8	.5	17.2
108	109	70	83.6	72.	3.8	.5	17.2
114	110	71	84.7	72.	3.9	.5	17.2
120	110	71	84.6	72.	3.9	.5	17.2
126	109	70	83.6	71.	3.8	.5	17.2
132	109	70	83.6	71.	3.8	.5	17.2
138	109	70	83.7	72.	3.8	.5	17.2
144	110	71	84.7	72.	3.9	.5	17.2
150	110	71	84.6	71.	3.9	.5	17.2

B.P. Systolic	=110 mmHg	Right atrial press.	= 11.9 mm Hg
Diastolic	= 71	Mean capill.press.	= 20.4 mm Hg
Mean	= 84.6	Cardiac output	= 3.9 l/min
Heart rate	= 71.	Stroke volume	= 54.0 ml

Figure 10. Display of numerical results.

select the option 3. You can choose either the standard chart and tables of values, or list eight selected haemodynamic variables in columns during the course of the simulation, as shown in Figure 10, instead of the standard graphical display.

4. Suggested experiments

1. Assume that total heart work ≈ cardiac output × mean pressure difference between aorta and right atrium, and that nitroglycerine dilates arteries and veins in roughly equal proportion. What does nitroglycerine do to: (a) cardiac output, (b) the work of the heart? (alter factors 1 and 2).
2. Produce a fairly severe blood pressure reduction by three means: (a) haemorrhage (reduce factor 5, blood volume); (b) diminished myocardial contractility (reduce factor 3); or (c) diminished arterial resistance, e.g. adrenergic blockade (factor 1 to be reduced). What is the main haemodynamic difference between the three states, and how may such states, especially haemorrhage and myocardial disease, be distinguished clinically?
3. What limits the rise of blood pressure produced by excessive arteriolar constriction? (increase factor 1). Progressively raise arterial pressure by

this means. Why do you never see a patient with a systolic blood pressure of 400 mm Hg?

4. What is the mean pressure filling the circulation? (This can be determined by killing a patient and looking at the residual pressure.) Can you see, from this consideration alone, why a 3000 ml haemorrhage would be fatal? (Repeat the experiment changing blood volume – factor 5.)
5. One of the ways of producing the syndrome of right or congestive heart failure in an animal is by tight constriction of the inferior vena cava in the chest. You can simulate this in *MacMan* by progressively increasing venous resistance, keeping all other factors constant. Examine the results. Can you see why this manoeuvre should lead to fluid retention, progressive congestion of the systemic circulation and ultimately to oedema?
6. Why does a large increase of cardiac contractile (i.e. pumping) ability not produce proportional changes in the output of the heart? Contrast the effect of progressive increase in cardiac contractility with those of progressive increase in blood volume. Why are the responses so different? Certain compounds increase cardiac contractility: what are the haemodynamic circumstances in which they would work particularly well?
7. Congestive heart failure is commonly associated with reduced cardiac contractile function and increased blood volume. Simulate this situation in *MacMan* by progressive reduction of cardiac contractility and progressive increase in blood volume, trying to maintain a sufficient systemic arterial pressure to keep the coronary circulation going. What symptoms and signs develop as this manoeuvre is progressively extended? How do they correspond to the real life situation?
8. What is the effect of 'Valsalva's manoeuvre', i.e. blowing up a column of mercury and holding it for a while, thus increasing intrathoracic pressure? Start with a small increase of intrathoracic pressure, e.g. 2 – 4 mm Hg positive pressure. In what way is *MacMan* different from a normal subject? What might explain the difference?
9. To what extent can you transfuse *MacMan*? Progressively increase blood volume by increments of 500 – 1000 ml. Why does this manoeuvre have such a small effect on systemic arterial pressure? What eventually kills the subject? Does this ever happen in clinical practice?
10. Examine the effects of progressive haemorrhage. Does it make any difference whether blood loss is fast or slow? What eventually kills *MacMan*? What haemodynamic consequences follow on prolonged sustained hypotension? What symptoms and signs would be expected from blood loss?
11. Examine the effects of resetting baroreceptor sensitivity to that of a hypertensive patient. (This option is available if you ask to change baroreceptor function and say that you do not want to cut the buffer nerve). Having established the circulation of a hypertensive subject, examine the performance of the baroreceptor stabilising system by altering arterial resistance, cardiac contractility and blood volume. Why is it so much easier to raise blood pressure and sustain it in this way by baroreceptor resetting than by increasing blood volume, cardiac contractility or arterial resistance directly?
12. What is the effect on blood-pressure stabilization of cutting the buffer nerves? Does any residue of blood-pressure stabilization remain after this manoeuvre, i.e. is the expected change in blood pressure produced by transfusion and haemorrhage the same as would be expected from a completely passive system?
13. By now you should have acquired a lot of data on an intact *MacMan*, probably enough to enable you to examine the operation of the blood-pressure stabilizing system in detail. Can you work out the means by which blood pressure is stabilized through the nervous system, i.e. what factors controlling blood pressure are influenced by the level of blood pressure itself?
14. Examine the operation of the systemic arterial-pressure stabilizing system in terms of the range of blood pressure over which stabilization can occur. How much of *MacMan's* arterial resistance is fixed and not normally variable? To what extent does the range and sensitivity of the stabilizing system in *MacMan* conform to that observed in experimental animals and in man?
15. Produce pulmonary oedema by progressively increasing blood volume and also, if you wish, by decreasing cardiac contractility. There are several lines of treatment which will lower capillary pressure, prevent lung engorgement and relieve shortness of breath, and which can be simulated in *MacMan*. What are these possibilities? Which is ineffective in *MacMan* and why does it not work?
16. The capacitance of *MacMan's* circulation has been assumed to lie on the venous side of the circulation. To simplify the model, it has been assumed that the pressure acting to distend the veins is the average of the central venous pressure and the mean capillary pressure. Capacitance is a measure of the pressure/volume relationship of the system, i.e. the volume that the system can contain at a given pressure. From a knowledge of the normal residual effective volume of the circulation, derived from solving problem 4 above under different conditions, can you determine the range of variation which can take place in circulatory capacitance with different stresses? Can you derive a formula to predict the circulatory capacitance from a knowledge of the other variables? (This is an intellectually difficult problem, though it is soluble by sufficiently ingenious experiments!)

Note that you can modify venous capacitance using factor 6 in the model (see Section 2.3).