Hitting the Target — with monoclonal antibodies

Contents: Reading and questions concerning the production and uses of monoclonal antibodies.

Time: 1 to 2 periods.

Intended use: GCSE Biology and Integrated Science. Links with work on disease and functions of the blood. More suitable for use with students likely to achieve grades A to C at GCSE.

Aims:

- To complement and revise prior work on the body's defences against disease
- To develop awareness of an important aspect of biotechnology, the production and uses of monoclonal antibodies
- To illustrate the process of scientific discovery and the technological potential of such discoveries
- To provide opportunities to practise skills in reading, comprehension and problem-solving.

Requirements: Students' worksheets No. 609

Background notes on monoclonal antibodies

The information given in the students' materials is highly simplified. In particular, production of antibodies is much more complex than how it is presented in the students' worksheets. It involves two types of lymphocytes, T cells and B cells. The T cells rapidly increase in number and then help the appropriate B cells increase in number. The B cells then produce the correct antibody. The process is not completely understood and is still an area of controversy.

Producing monoclonal antibodies in the laboratory is also more complex. The tumour cells used, for example, are deficient in an enzyme and could not survive without fusion with a lymphocyte. Because of the method of making the monoclonal antibodies, a number of different types of lymphocyte-tumour combinations are produced, as well as lymphocyte-lymphocyte and tumour-tumour combinations. The combination of interest has to be separated from the others.

Notes on some of the questions

Q.1 Having once been exposed to a particular pathogen, lymphocytes will respond more quickly to a subsequent exposure, and will rapidly produce the necessary antibodies and thus prevent the disease developing.

Q.2 Chicken-pox and measles are both viral diseases, but each requires a specific antibody.

Q.3 In the case of colds there are so many different forms of the virus responsible that it is impossible to gain immunity to all of them.

Q.5 See 'Background notes on monoclonal antibodies' above.

Notes on the problems

The problems are graded in approximate order of difficulty, easiest first. The 'solutions' given below are those that have been actually adopted, though students may produce other plausible solutions.

Problem 1 Make monoclonal antibodies specific to the protein (which is actually the hormone human chorionic gonadotrophin, HCG). Add antibodies to the urine and arrange for a suitable indicator to be present which will change colour in the presence of the HCG-antibody complex. (In fact, the kit contains a 'stick' impregnated in suitable antibodies. The stick is held in the urine, then dipped in an indicator solution.)

Problem 2 The bone marrow is removed and treated with monoclonal antibodies targeted on the cancer cells. These monoclonal antibodies have ricin attached to them.

Problem 3 Make monoclonal antibodies which are specific for Factor 8 and use them to pick out Factor 8 from blood. The antibodies are immobilized in a column through which the blood passes. Factor 8 attaches to these antibodies, and can later be removed from the column.

Problem 4 This problem is presented in a more open-ended way, and students may not arrive at the exact answer given here. The method used is to attach a weakly radioactive isotope to an antibody which is targeted on the cancer cells. Finding where the radioactivity is most concentrated then tells the doctor where to direct treatment.

Acknowledgements Figures 1 and 8 supplied by Imperial Cancer Research Fund.

HITTING THE TARGET with monoclonal antibodies

What are antibodies?

Antibodies are made by the body in response to attack by bacteria or viruses. This helps protect against infection. The antibodies do this by recognizing very accurately the proteins on the surface of the bacteria or microbe. Antibodies are produced by cells. By growing these cells in the laboratory, it is possible to produce large amounts of one type of antibody. These are known as **monoclonal antibodies.** To understand how this is done, let's first examine the body's natural mechanism for making antibodies.

Figure 1 Using an electron microscope to examine the action of antibodies

Where are antibodies made?

Antibodies are made by special cells called **lymphocytes.** Lymphocytes are made in the lymph nodes and spleen. You may have felt lumps in your armpits or on the side of your neck when you are ill. These are the lymph nodes hard at work producing antibodies to fight your illness. The lymph nodes can produce tens of thousands of different lymphocytes. Each one is able to produce a different antibody if necessary.

How do antibodies work?

Every microbe has uniquely shaped proteins on its surface. These proteins are called **antigens.** Antibodies have shapes which can lock onto a particular antigen. In this way antibodies recognize antigens, and attach themselves to them (Figure 2 on the next page).

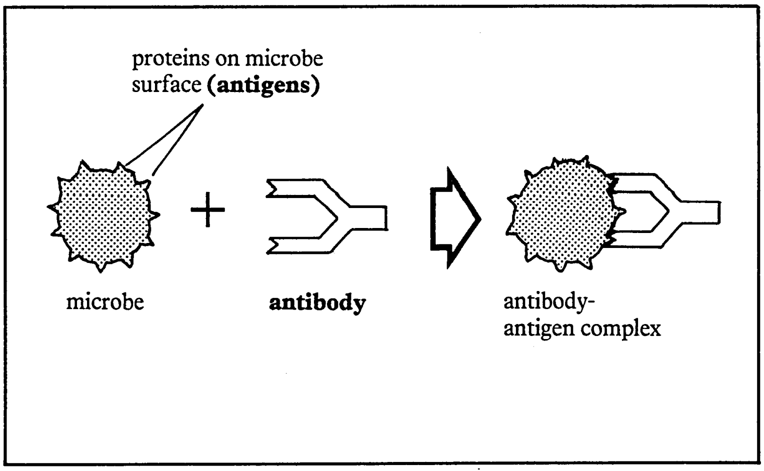

Figure 2 The antibody-antigen interaction

Whatever the shape of the antigen, an antibody exists which will fit it and make it harmless. The antibody-antigen complex can then be ingested and destroyed by the body's 'scavenger' cells — the **phagocytes** (Figure 3).

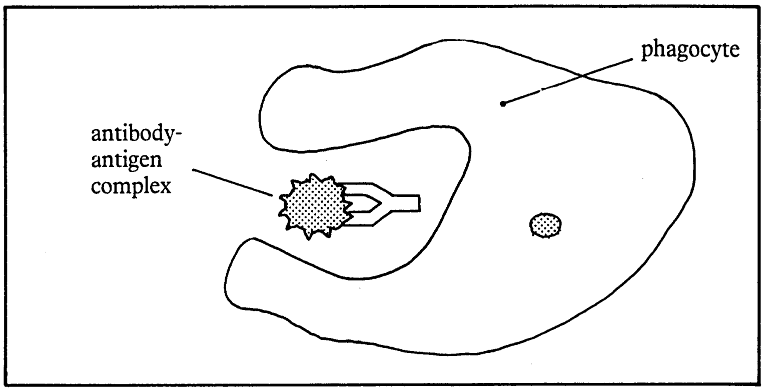

Figure 3 A phagocyte ingesting an antibody-antigen complex

Manufacturing antibodies

The body is usually invaded by thousands of microbes of the same type. So the body must be able rapidly to increase the production of the necessary lymphocytes.

As soon as new antigens are spotted in the body, action begins. The body rapidly increases the numbers of the lymphocytes that have the right shaped antibodies to lock onto the invading antigens. Many of these 'right shaped antibodies' can then be quickly produced. Only by this rapid response can the infection be successfuly fought (Figure 4 on the next page).

Questions

1. *For many diseases, once you have had the disease you are* **immune** *and cannot catch it again. Explain why.*
2. *Explain why antibodies produced to fight chicken-pox do not work against measles.*
3. *Suggest a reason why we do not get immune to colds.*

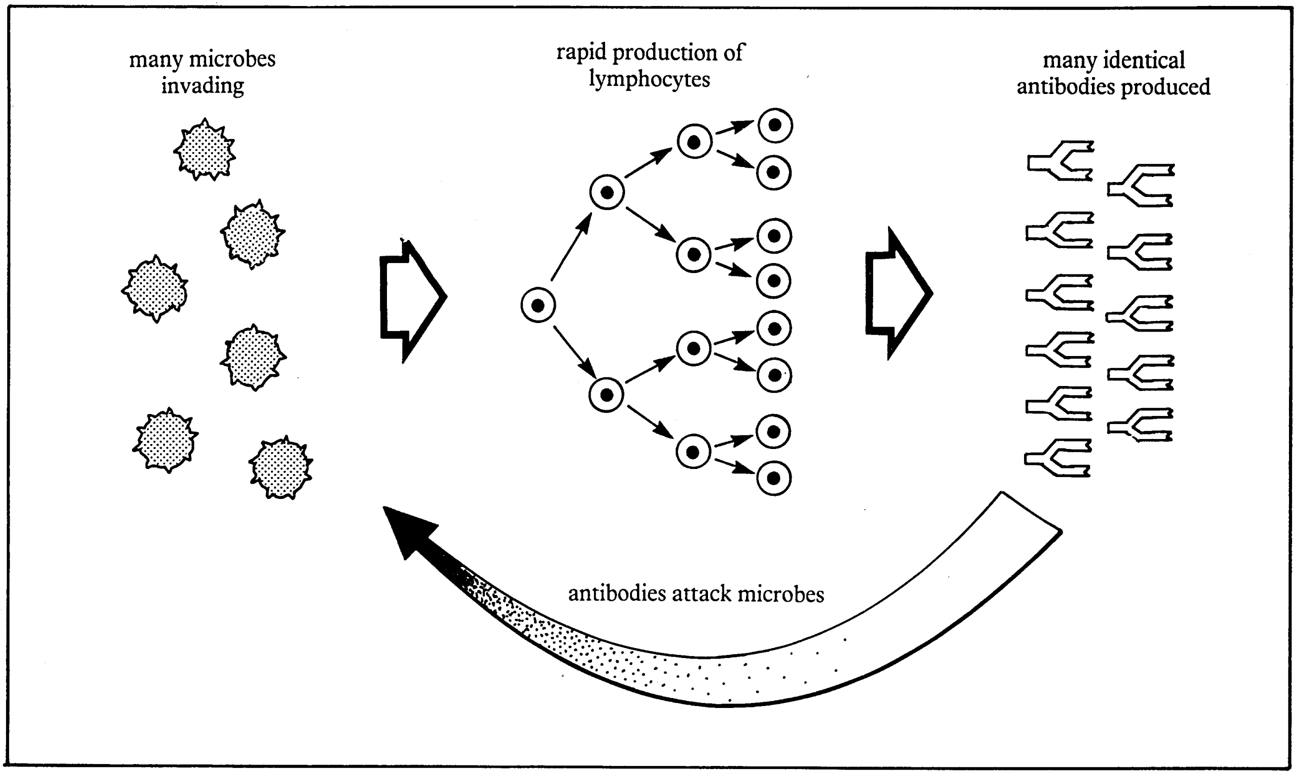

Figure 4 Manufacturing antibodies to fight invaders

Monoclonal antibodies

When large numbers of identical cells are produced they are called **clones.** When large numbers of *one type* of cell are produced, these cells are called **monoclonal.**

Scientists were interested in studying the antibody produced by a single type of lymphocyte. To do this, they had to persuade a lymphocyte to reproduce outside the body. It would then produce plenty of one type of antibody for them to study.

How are monoclonal antibodies produced in the laboratory?

Two Cambridge scientists, Cesar Milstein and George Kohler, were the first to produce monoclonal antibodies in the laboratory. In 1984 they received Nobel prizes for their work.

The big problem they had to overcome is that lymphocytes rapidly die outside the body. Milstein and Kohler had to persuade lymphocytes to go on living and reproducing in a test tube. To do this they used tumour cells. Tumours inside the body can be a serious problem and some tumours cause cancer. But tumour cells are able to go on living and reproducing outside the body. The scientists used them to make 'hybrid' cells. These 'hybrids' could produce antibodies like lymphocytes, but live outside the body like tumour cells.

Figure 5 illustrates the method.

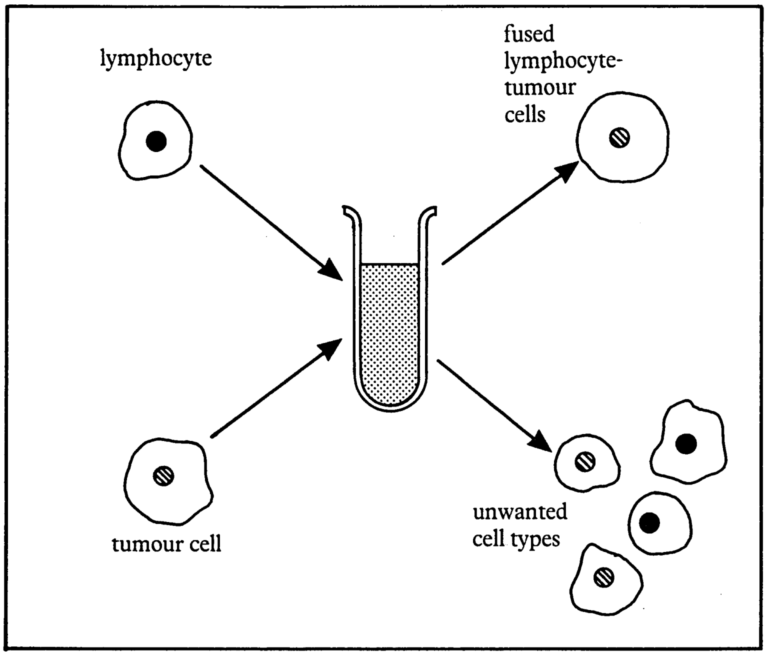

Figure 5 Making lymphocyte-tumour cells

They took lymphocytes from the body and mixed them with tumour cells in a test tube. They added a chemical to lower the surface tension, and gently shook the mixture. The lower surface tension allowed the cells to fuse (join together). Some of the lymphocytes fused with tumour cells. This 'hybrid' of lymphocyte and tumour cell was able to reproduce and live outside the body. All the scientists had to do then was separate the cells they wanted from the ones they did not. The 'hybrid' lymphocyte-tumour cells could then be used to make monoclonal antibodies.

Questions

4 *Explain in your own words why hybrid tumour-lymphocyte cells were used instead of ordinary lymphocyte cells.*

5 *After shaking tumour cells and lymphocyte cells together, the scientists had to separate the cells they wanted from the cells they did not want. Which cells did they want? What unwanted cells would have been present?*

Why the method was important

Milstein and Kohler originally made their monoclonal antibodies for scientific experiments. But it was soon clear that they would have important uses in medicine.

Antibodies work by recognizing a protein on the surface of a particular cell, and locking onto it. This means a particular cell can be made the 'target' of an antibody 'attack'. The antibody will attack that cell and no other.

Targeting drugs

For example, a drug could be attached to a monoclonal antibody. The antibody would be 'targeted' against proteins on a diseased cell. In this way the drug would be delivered to the diseased cell by the antibody (Figure 6). The drug would be concentrated in the area where it would do most good, instead of being spread throughout the body. This means that lower doses of the drug could be used.

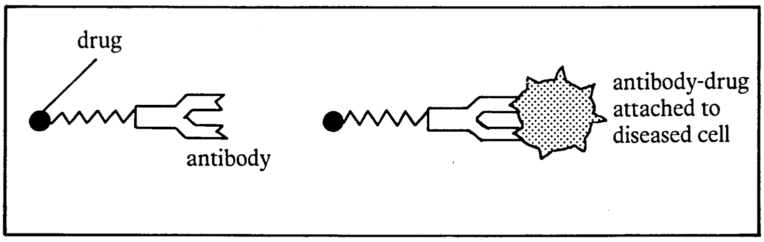

Figure 6 Targeting a drug using a monoclonal antibody

Purifying proteins

Monoclonal antibodies are not just used to destroy cells. They can be used to pick out useful substances from a mixture. Suppose you want to separate one protein from a mixture. An antibody is made which will pick out the required protein (Figure 7).

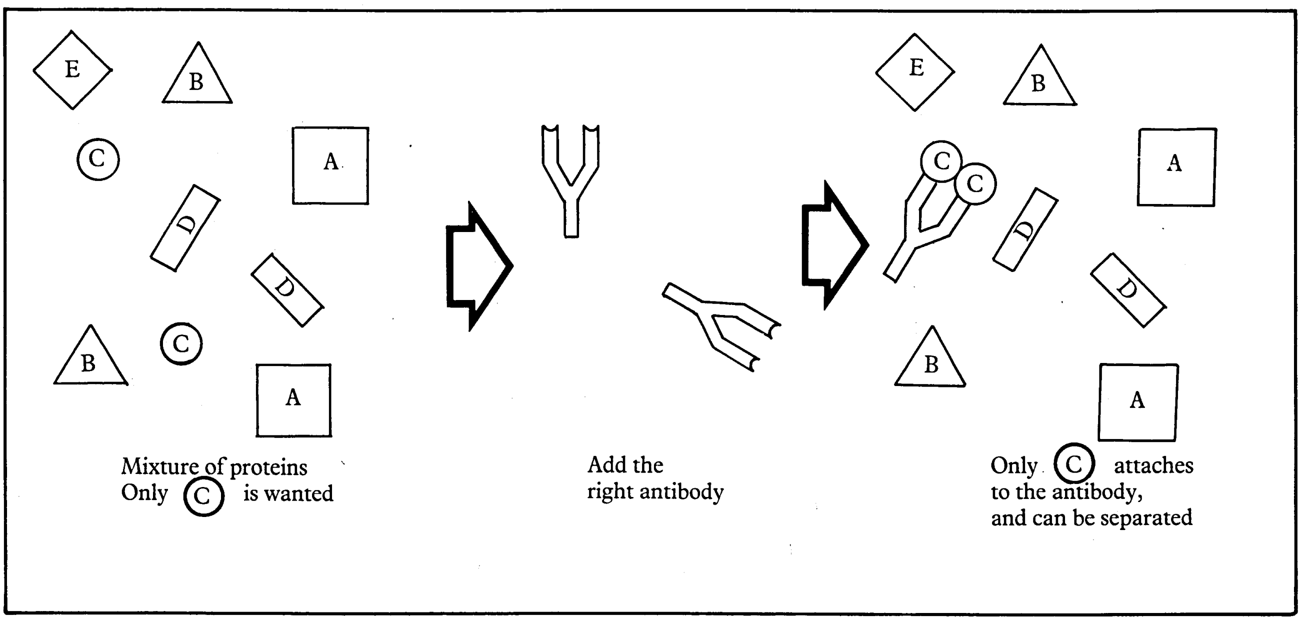

Figure 7 Using monoclonal antibodies to separate proteins

Detecting diseases

Kits can be produced which detect disease quickly and accurately. They contain monoclonal antibodies which react with antigens present on the microbe causing the disease. A solution containing the antibodies is added to a sample of the patient's blood or urine. If the microbes are present, the antibodies react with them. This in turn causes another chemical to change colour. The colour change indicates the patient has the disease.

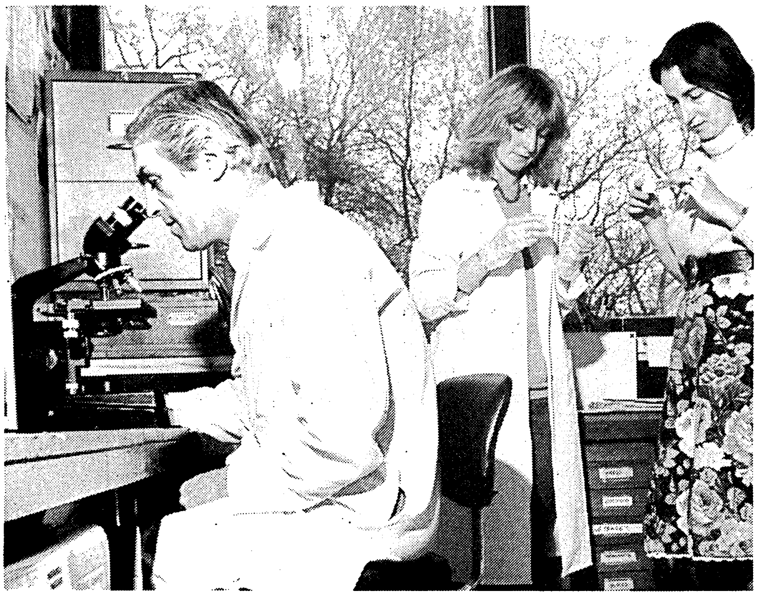

Figure 8 These research workers are examining lymphocyte-tumour hybrid cells

Solving problems using monoclonal antibodies

These are all real-life problems that have been solved using monoclonal antibodies. In each case, suggest a solution.

Problem 1 Pregnancy testing During pregnancy, certain proteins are released into the urine. How could monoclonal antibodies be used in a pregnancy testing kit?

Problem 2 Treating leukaemia Leukaemia sufferers have cancer cells in their bone marrow. These cells can be killed using a deadly poison called ricin. Unfortunately, ricin also kills normal bone marrow cells. How could monoclonal antibodies help?

Problem 3 Treating haemophiliacs Haemophiliacs have blood which does not clot. They risk bleeding to death when they cut themselves. This is because they lack a protein in their blood called Factor 8. Factor 8 is vital to the blood-clotting process, and haemophiliacs can be treated by giving them Factor 8. This can be done by giving them a transfusion of normal blood, which contains Factor 8. However, this means going to hospital, and there is always a chance that the blood given may contain harmful viruses, such as the virus that causes hepatitis. A better plan is to give haemophiliacs an injection of concentrated Factor 8. How could monoclonal antibodies be used to get pure Factor 8 from blood?

Problem 4 Finding cancers Before doctors can treat a cancerous growth, they need to know exactly where it is in the patient's body. Sometimes this is difficult to find out, even using X-rays. How could monoclonal antibodies help?

Robots at Work

Contents: Reading, questions and discussion on industrial robots and their future implications.

Time: 1 to 2 periods.

Intended use: GCSE Physics, Technology and Integrated Science. Links with work on feedback control and sensors.

Aims:

- To complement work on control and sensors
- To introduce the topic of industrial robotics, and to show some of the advantages and limitations of the use of robots
- To develop awareness of some of the implications of industrial robotics, particularly with reference to employment
- To provide opportunities to practise skills in reading and comprehension, and the ability to communicate an argument.

Requirements: Students' worksheets No. 610

Notes on the activity and questions

The activity and questions are best tackled by students working in pairs or small groups, since this will encourage them to discuss ideas with one another.

Activity — Shall we buy a robot? This activity is intended to give students an opportunity to exercise their powers of communication and argument, though the level at which it is answered is likely to vary greatly according to ability.

(a) Students should make some mention in their note to the board of directors of the expected payback time for the robot — the time in which the initial cost of installation will be recovered.

(b) This is a more difficult task than (a), but a very important one. Companies introducing new technology find that all is wasted unless the people who are going to operate it and work in associated areas are consulted first.

Mention could be made of the unpleasant nature of the job being replaced, and of the fact that the robot will require a certain amount of human supervision. It would also be worth mentioning that the robot should help provide the high quality needed to keep up with competitors and avoid loss of markets.

Q.4 In the long term, 'intelligent' robots could take many more jobs from humans. This could be seen as both a threat and an opportunity: a threat to jobs, but an opportunity for people to follow more fulfilled lives using increased leisure time. Robots after all create the same amount of wealth as the workers they replace, and if the wealth is distributed appropriately, people's standard of living will be the same as before, but with increased leisure. Students will undoubtedly also want to discuss the possibility of malevolent intelligent robots 'taking over' control of human affairs.

Other resources

Robots in Industry is a useful film on the subject, produced by the Department of Trade and Industry. It lasts 27 minutes and is available on 16mm film or video. It is primarily intended for industry, but is also suitable for school use. Available on free loan from: Central Film Library, Chalfont Grove, Gerrards Cross, Bucks SL9 8TN.

The Institution of Electrical Engineers has produced a poster, *Electrical Engineering — ROBOTS,* and a useful booklet, *ROBOTS — notes for the guidance of teachers.* Available from: Schools Liaison Service, Institution of Electrical Engineers, Station House, Nightingale Road, Hitchin, Herts SG5 1RJ.

Acknowledgements Figure 1: data from the British Robot Association; Figure 2 is reproduced by permission of *Understanding Electricity* (The Electricity Council); Figure 3 is adapted from *A Human Guide to Robots* (Department of Trade and Industry); Figure 4 is reproduced by permission from *Technology Made Simple* by Don McCloy (Heinemann); Figure 5 is reproduced by permission of Unimation (Europe) Ltd; Figure 7 is reproduced by permission of GEC Electrical Projects; Figure 8 supplied by Cincinnati Milacron (UK).

ROBOTS AT WORK

The word 'robot' may make you think of space-age fantasies like R2 D2, or of Frankenstein's monster. Yet there are hundreds of robots in Britain, and the robot population is growing (Figure 1). The robots we will be looking at in this unit are very down-to-earth, hard working machines called **industrial robots.**

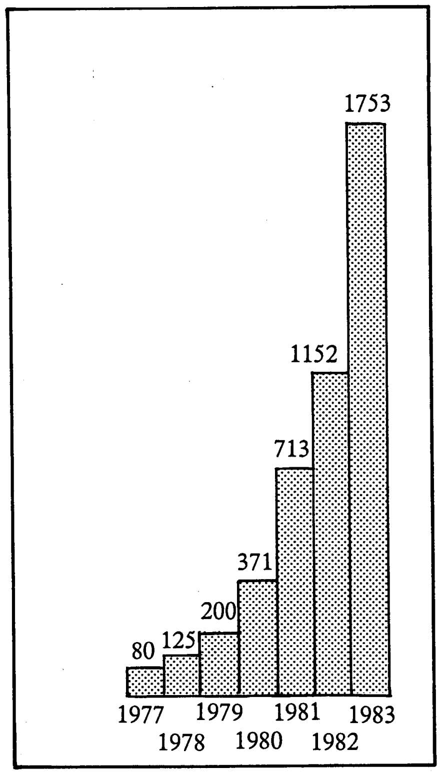

Figure 1 Growth in the robot population of Britain from 1977 to 1983

What is an industrial robot?

Suppose you are a car manufacturer. You need to make literally thousands of different parts for your cars. Making these parts and putting them together can be very boring and perhaps unpleasant work for humans.

Take one small example. Part of the wheel bearing is a complicated metal spindle which is cast from molten steel (Figure 3).

The newly-cast spindle has sharp edges which must be removed by polishing. This can be a dangerous job because of the small, sharp pieces of metal which fly off. It is also very boring. But because of the complicated shape of the spindle, it is difficult to build a machine to do the job.

This is where robots come in. A robot can be 'taught' to do the job. It will then follow the complicated shape with a polishing machine held in a mechanical hand. Robots do not get tired or bored, and they do not mind unpleasant working conditions. What is more, a robot can be programmed to do different jobs. For example, if the shape of the piece of metal was changed, the robot could be reprogrammed to follow its new shape.

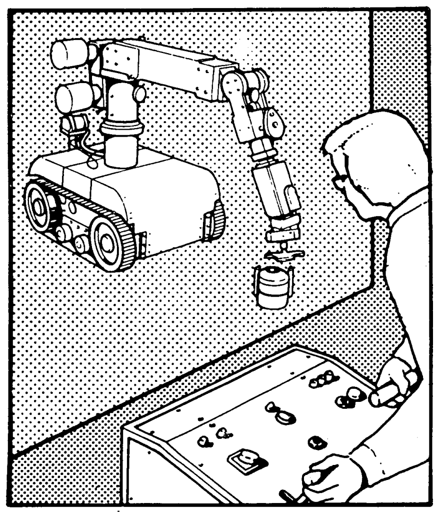

Figure 2 One of the earliest uses of industrial robots was for handling dangerous radioactive materials

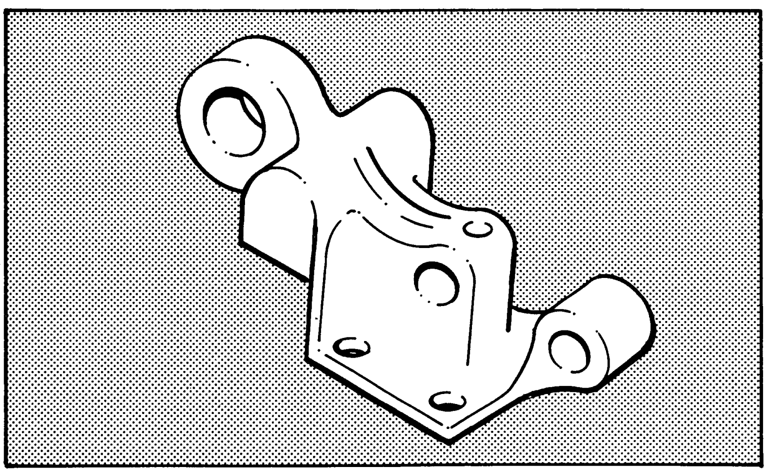

Figure 3 A spindle cast from molten steel

What do industrial robots look like?

Industrial robots do not look much like the ones you see in space fantasies. They usually have no head, only one arm and are fixed to the floor. Figure 4 on the next page shows a typical example.

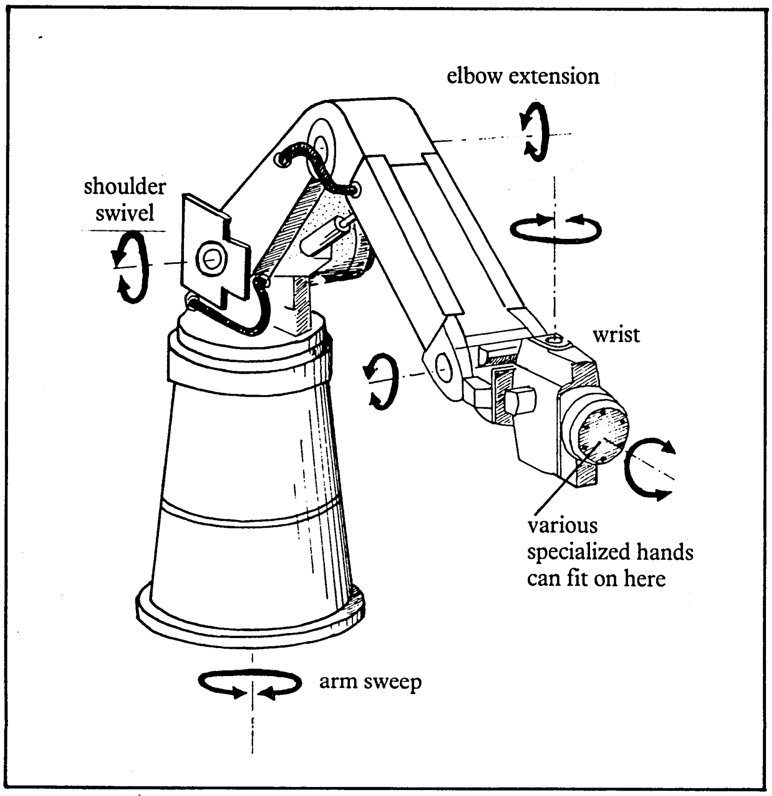

Figure 4 A typical industrial robot

Notice the different ways the robot's arm and hand can swivel. This makes them as manoeuvrable as a human's. The movements are controlled by a microcomputer inside the robot. The computer can be programmed to take the arm and hand through a fixed series of movements.

Not all robots look like this one. For example, a few moving robots have been developed, like the robots used to explore in space.

How do robots work?

Suppose a robot is being used to lift sacks off a conveyor belt, as in Figure 5. A suction pad is used to lift the sack. The robot needs to know when the pad is in position on the sack and ready to lift. This is done using **feedback control** (see box on next page). A pressure sensor tells the robot's microcomputer when there is enough suction to lift the sack. The microcomputer then tells the arm to lift it.

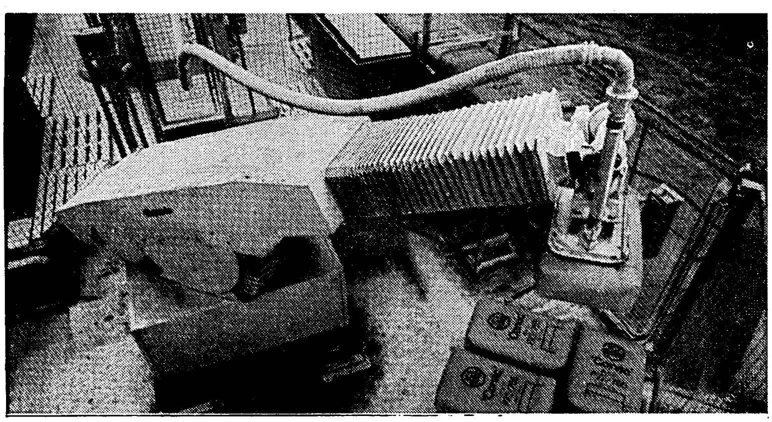

Figure 5 A robot lifting sacks off a conveyor

What is feedback control?

Try drawing a circle on a piece of paper, with and without your eyes closed. The result is much better with your eyes open. Your eyes can help control where your hand goes.

Your eyes are **sensors** which pick up information. They **feed back** this information to the brain, which is the **controller.** The brain uses the information to control the hand, which is the **actuator** (Figure 6).

Feedback control has many everyday applications. For example, it is used to control the temperature of a centrally-heated house. Here the sensor is a thermostat, which feeds back information to the heater control box, and switches the heater (the actuator) on and off.

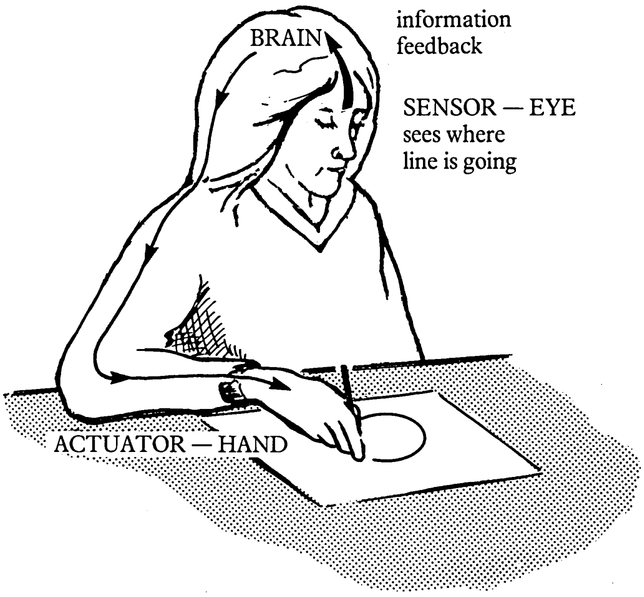

Figure 6 Feedback control helps you draw

Robots use feedback control to make sure their movements are right. This means they need sensors, a control centre and an actuator.

Sensors

These might be:

- pressure sensors
- touch sensors
- strain gauges, to test loads
- induction coils, to sense when metals are nearby
- light sensors.

Robots are now being developed which use video cameras to sense where things are — a 'robot eye'.

Control centre

The control centre of the robot is a microcomputer, situated safely inside the body. The computer can be programmed to take the robot through a series of moves. Feedback information from the robot's sensors tells the computer when the hand is in the right position. The robot can be made to do different jobs, by reprogramming the computer.

One way of programming is to get a skilled worker to 'teach' the robot by leading it through the job (Figure 7). For example, a skilled paint sprayer might lead the robot hand through the right movements for a particular spraying job — say on a car door. The computer 'brain' remembers the series of movements. The robot can then paint car doors endlessly until it is reprogrammed.

Figure 7 'Teaching' a robot

Actuators

The robot hand is the part that does the job. It may be powered by electricity, by hydraulics (pressurized liquid) or by pneumatics (pressurized gas). Different special-purpose hands can be used — for gripping, for lifting with suction pads, for drilling, welding, paint spraying and so on.

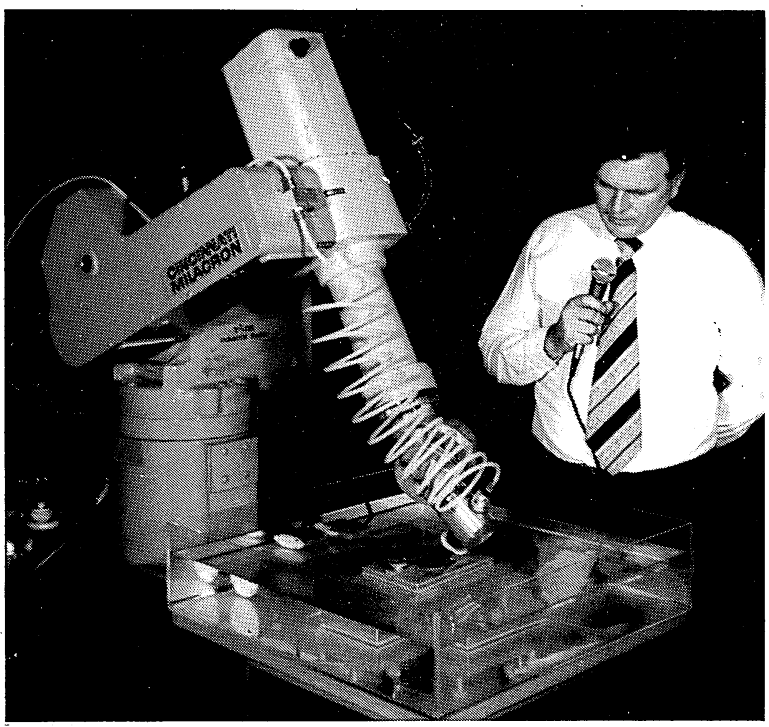

Figure 8 This robot engraves glass blocks. It can recognize the human voice, and is controlled by spoken commands.

Do robots take jobs from humans?

Robots do take jobs from humans, but it is usually the unpleasant jobs. Industrial robots are ideal for jobs that are dangerous, unhealthy or unpleasant — for example, handling acids, or working in very hot places. They are good at boring, repetitive work. Often they do the work better than humans, because they are more precise and do not lose concentration or have an 'off day'. But they are not very clever, because they only do what they have been told to do.

Robot experts are working on 'intelligent' robots, which can learn from experience and make decisions. These robots depend on very powerful computer 'brains'. But at the moment really intelligent robots are still a long way off. When they do come, they may be able to take over still more jobs.

Some people say robots may cause mass unemployment in the future. Others say they will only take the nasty jobs that no one wants anyway, and that they will create new jobs and give people more leisure time. What do you think?

Activity — Shall we buy a robot?

It is best to work on this in pairs or small groups.

Imagine you are Production Manager for a firm which makes ovens. Each oven must be sprayed with enamel on the inside (Figure 9). The spraying job is unpleasant and boring. It is difficult for workers to get the even coating that is needed. You are anxious to do everything you can to keep the quality of your products high. If you do not, you may lose orders to foreign manufacturers.

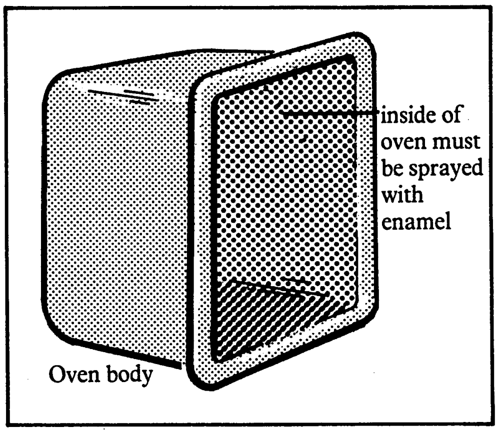

Figure 9

You are interested in using a robot to do the spraying. You have investigated this possibility, and discovered the following points:

- The robot is expected to do a more reliable job than a human worker and to spray more evenly.
- The robot would cost about £43 000 to install.
- The robot would cost about £2500 a year to repair and maintain.
- The robot would replace two workers, though it would need a part-time human supervisor. There would be a saving of about £23 000 a year on wages.
- The robot is expected to last about ten years before it needs to be replaced.

(a) Before you can buy the robot, you need to persuade the firm's board of directors to approve the purchase. Write a short note to the board, explaining the advantages to the firm of buying the robot.

(b) You also need to explain to your workers why you want to bring in the robot. Remember this will mean a loss of jobs. Write a short note to the trade union representative explaining the advantages to the workers of bringing in the robot.

Questions

It is best to work on these in pairs or small groups.

1 *Here is a list of jobs. For each job, say whether you think it would be suitable for replacing a human worker by a robot. Explain your answers.*
  (a) Soldering wires onto a circuit board
  (b) Cleaning a house
  (c) Hairdressing
  (d) Sorting and packing eggs
  (e) Hospital nursing
  (f) Driving lorries.

2 *Think about the robots described in this unit.*
  (a) What do they have in common with human workers?
  (b) What differences do they have compared with human workers?

3 *Scientists are interested in using robots to explore deep under the sea.*
  (a) Why are robots particularly suitable for this kind of exploration?
  (b) In what ways would robots for this kind of exploration need to be different from the ones described in this unit?

4 *Robot experts are now trying to develop advanced robots. These robots would be more intelligent, have better senses and be able to do more of the things that humans can do.*
  (a) What advantages can you see in developing robots that are more like humans?
  (b) What disadvantages can you see in this kind of development?

SATIS 6

List of units in this book

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