On the uses of analogy

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ON THE USES OF ANALOGY

Dr. A.J.P. MARTIN, F.R.S.

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INAUGURAL ADDRESS BY
DR. A.J.P. MARTIN, F.R.S.
BY APPOINTMENT OF THE
"STICHTING EINDHOVENS HOGESCHOOLFONDS"
EXTRAORDINARY PROFESSOR
OF THE TECHNOLOGICAL UNIVERSITY
OF EINDHOVEN

FRIDAY, MARCH 13, 1964

Members of the Board of Trustees,
Mr Secretary of the University,
Mr President and Governors of the "Stichting Eindhovens Hogeschoolfonds"
Members of the Senate,
Members of the academic, administrative and technical staffs,
Students,
Ladies and Gentlemen,

It is with pleasure, pride and surprise that I find myself giving this inaugural lecture. Pleasure and pride at the fulfilment of an ambition to be a professor, that I first felt as a young man at Cambridge, though at the time I eschewed teaching, feeling that it would take too much time from the pursuit of the research that I was so anxious to pursue. Apart from that I did so poorly in my examinations that I should have found it difficult to obtain any teaching post. My connection with a university ceased when I left Cambridge in 1938 for the Wool Industries Research Association; and I have increasingly regretted the fact that I have been cut off from university life ever since.

The surprise is at finding myself a Professor of the theory of Analogy. I fear that if you have come to learn about this I have little to teach. But none the less I have come to realise that it is a subtle choice of title for such a professorship, since the use of analogy is spread through all science, in that it is an essential part of at least one of the main methods of science, that of providing hypotheses for test.

In extending any science there are two essential steps. Making an hypothesis and testing it. The hypothesis serves to relate known facts and to make predictions that may be tested. Untestable hypotheses add nothing to knowledge. No scientist can ever claim absolute and incontrovertible truth for his hypotheses, which are always liable to be overthrown by experiment. There is no place for reverence in science. As a result of their method, scientists know far more about truth than those who study other subjects (This doubtless is an unscientific observation).

It is part of the scientific method that no elaborate superstructure must be built on unverified hypotheses, and this severely limits the use of analogy. I have myself used the analogy with distillation to produce a theory for countercurrent extraction (which had already been done) and for chromatography, which proved illuminating. My distinguished predecessor in this chair applied the analogies with communication problems to chromatography with extremely fruitful results. Perhaps his type of operation was exactly what was intended by the founders of this chair. But as the English courts in interpreting a law take into account only what the law says and pay no attention to what Parliament intended, so I feel free to interpret analogy as I think fit. I was surprised to find that there was already a scientific journal in my subject circulating in England and America called Analog, which has already been going for several years. It has however a subtitle "Science Fact and Science Fiction" which illustrates perhaps some of the dangers of the uncritical use of analogy.

In many fields of science and technology it is the simple basic ideas which are at once the most rewarding, and the hardest to find. But before they can be of value they must be supported by a structure of mathematics, in the case of physical ideas or a number of subsidiary inventions or pieces of hardware in the case of a technological problem. Often these subsidiary problems are no harder to solve than those of trivial importance, but solved they must be if the original idea is to be brought to fruition: it is no doubt the necessity for the detailed working out of the subsidiary problems that causes such delay at times in the development of widely known ideas.

Most of my scientific life has been concerned with developing methods of separating similar substances. As a schoolboy I constructed a distillation column 2 metres long (packed with sieved coke) by soldering together empty coffee tins, and I went to Cambridge with a better knowledge of distillation than anyone I met there during the next ten years.

The theoretical plate concept arose naturally in distillation since the early columns consisted of a wide tube with a succession of horizontal plates, just perforated, or provided with bubble caps at which it was hoped that liquid and gas would come into equilibrium. In fact equilibrium was not reached, but it was found that the behaviour of the column could be well described in terms of a number of "theoretical plates" less than the actual number that the column contained. Within each theoretical plate perfect equilibrium was assumed. Peters in 1922 showed that packed columns could be equally well described in terms of theoretical plates, a section of a column constituting a theoretical plate when the vapours issuing from the top of the section had a composition in equilibrium with the liquid issuing from the bottom of the section. The application of the idea to liquid countercurrent extraction required no change of concept, but to use countercurrent extraction as a method of separation requires the use of half of the column as the equivalent of the condenser of a distillation column. I can still remember the feeling of satisfaction as I deduced this while walking home to lunch from the laboratory, though I was by no means the first to do so. Later I applied the theoretical plate concept to chromatography. Its chief value has been to make the subject of chromatography easy to understand, and rescue it, at least to some extent, from the grasp of mathematicians.

A somewhat modified plate method can be used to predict the performance of diffusion column. These have been little used except for the separation of isotopes but I believe that a little engineering development is all that is required to make the method of value to the biochemist. I hope to be able to have a research student doing this work here.

Another method of separation which has interested me for 30 years is electrophoresis. I did some preliminary work in 1944 and again in 1946 on the electrophoretic analogue of displacement chromatography. Displacement chromatography was first clearly recognised by Tiselius and has been widely understood since. There is a precise analogy between ordinary chromatography and zone electrophoresis, which Consden, Gordon and I pioneered at the end of the war, and between frontal analysis and the Tiselius boundary electrophoresis method. But curiously no one has exploited the electrophoretic analogue of displacement chromatography though I have myself discussed it with many people and even given several lectures on it.

I hope to take up this method again with another research student.

My last illustration of the application of analogy is one of the broadest and simplest that is conceivable, the analogy between large and small. Scientific work is to a remarkable extent a matter of fashion. I have been fortunate enough to have been involved in starting a fashionable subject myself, namely chromatography. But a fashionable subject is not a comfortable one to work in. There is too much competition. Apart from its sheer ability to separate substances chromatography is remarkable for the small amounts it can handle. So small indeed that it becomes very difficult to put on to the chromatogram an accurate amount of material.

In this field, as in a vast number of others, there is difficulty in the purely mechanical aspect of handling. It is indeed true that almost throughout all science one would like to be able to work on a smaller scale than one is currently able to do.

It is curious that work by scientists on mechanical things is almost totally out of fashion. It is regarded as the proper field only for engineers and technologists. As a result the field of micromanipulation has been astonishingly neglected, being too small to interest engineers and apparently beneath the notice of scientists. Now that a large demand has arisen for small electrical components there is much work on making things smaller but the natural response has seemed to be to devise special methods for each problem. In another field where the direct need for a micromanipulator has been felt, in biology, people have accepted what I can only describe as stone age tools. Essentially just a spear and a battle-axe, and this in spite of the fact that for 300 years, since Van Leeuwenhoek's day, we have been able to look down a microscope. But the microscopist is still content with a tool with 3 or 4 degrees of freedom.

Now here is surely a case for the application of one of the simplest of all analogies. That between big things and small. For reasons I need not go into here, some three years ago I had the opportunity to spend a lot of time just sitting and thinking, following up a number of ideas that I had had but not properly digested. As a result I came to the conclusion that much the most important line I could follow would be that of making things smaller. The possibilities inherent in this unfolded only slowly and some of them were startling to me, so that it needed some courage to make them public.

Now when you sit down to think of it, there are certain very obvious methods which should be followed if you want to make things smaller. The first of these is that you should use small tools. It is not apparently obvious to everybody. I have been told more than once that people have found that to do a small job they needed tools even larger and heavier than usual to get the necessary accuracy. While this might seem to be a tenable view for something just a little smaller than usual, it is plainly untrue if we want to make things a thousand times smaller, and must be in fact untrue at all sizes. One has to make small but correspondingly accurate tools. One has not only to make them but to be able to use them.

Now there is, at least in conception, no difficulty in a small automatic lathe or other such machine tool. It will obviously work very much as its larger brother if you can successfully make it. In fact if you go into the theory of it you will find that if you keep linear speeds the same, and increase the accelerations inversely in proportion to the size, that all the parts will be similarly stressed, and pressures per unit area will be unchanged. Certain things of course do not scale down. The acceleration of gravity remains constant. As the size is reduced, gravity becomes therefore progressively less important. Surface tension remains constant and as curvature increases so surface tension becomes more and more important. For lubricants to work as before the viscosity should be reduced in proportion to size. Anything connected with diffusion, whether of matter or heat will become correspondingly more rapid. But though these things must be considered and allowed for, it seems unlikely that they will cause substantial difficulty.

The difficulty of manupulating the small tools remains formidable. If one considers how in fact one spends the greater part of the day in a workshop or laboratory, only a small part is found to be actually operating a tool. Much the greater part is spent in walking round, picking things up and putting them somewhere else. Often the man's function is merely that of feeding the machine, but this task is so varied and multifarious that only when very large numbers of parts are required is it reasonable to make machines to replace him.

Normally, what he does he does with his hands. For heavy objects he has mechanical aids. These however slow him down greatly, and for loads ranging from many kilograms to milligrams and less, transport is effected by his hands. The final positioning of the object is by the hands, and here again the hand is useful over an enormous range.

You can carry things kilometres and adjust them readily to one tenth of a millimetre and with more trouble to 1/100 of a millimetre.

If you count up the degrees of freedom of the hand and arm from the shoulder you will find that 27 degrees of freedom about covers all the important ones, but of course one does not use them all at once. To do the fine manipulations one rests one's hand and moves only the fingers. One can in fact, using tweezers, do assembly operations of astonishing delicacy. But even in normal life one is accustomed to make most complicated and delicate manoeuvres, for instance knitting, without thinking about it. In all this one is immensely helped by the fantastic number of sensory endings that one's hands contain.

Now clearly to operate our small tools we need small hands and arms, and equally clearly we cannot expect to make them as useful as the biological ones. What can we afford to dispense with and what can we not possibly make?

We are dictators of the world the machine will operate in, and it is probably possible that only limited movement corresponding to our feet is required. Stores can be arranged to be brought, as well as machines, or benches for hand tools, to the site of the manipulator.

The 27 degrees of freedom of the hand and arm are not too difficult to make though it may be questioned how far they are all necessary. Any equivalent of the sensory endings seems impossible to attain save for one, the torque exerted by each of the joints. It seems therefore possible and useful to try to construct a small hand with essentially the same number of joints as a real hand. It should follow exactly the motions of the real hand and tell one how much force one was exerting at each joint.

I imagine this to be done by putting one's hand into a kind of sleeve with glove attached operating a small hand and arm hydraulically, and each system for each joint to be provided with a hydraulic amplifying gear to exert on the real limb the appropriately magnified forces that are exerted by the small hand and arm.

It may be thought that it is unnecessary to provide so many degrees of freedom since six can provide any orientation and position in space and the addition of one or two more would be sufficient to enable the machine to pick up and put down what it was handling. You would in fact have to add coarse and fine adjustments and by the time you had made provision to be able to get at things from odd angles, I come to the conclusion that you would have something very little less complicated than a hand, as far as numbers of joints were concerned.

There is however another, I hope, great advantage in making the machine as like the hand as possible. If it works well enough one will be able to use it without having to learn. It will seem merely to be an extension of oneself. The extent to which one is incommoded by an injury to any part of the hand makes it obvious that one uses every part of the hand many times every day. If therefore we make a representation of a hand lacking essential parts we shall be adding unnecessarily to the amount we have to learn in using it.

The absence of sensory endings will result in our having something of the sensation of working in heavy leather gloves, something that does not gravely hamper one in driving a car, but does of course in assembling a watch. We should however be able readily to assemble a watch with our small hand, assuming its scale to be say 1/10 of our own hands. If the scale were still smaller we can expect to do things more delicately than we can with our unaided hands, and not to need the skill which delicate manipulations at present entail.

What therefore I think one should do, is to construct a manipulator of say 1/10 scale, and appropriate small tools and with these make a still smaller manipulator, which one could scarcely expect to make direct. It is in fact difficult enough to make even the 1/10 scale. If one makes a complete small workshop, then I believe one should be able to produce almost as wide a variety of objects from it as we can from workshops of normal size.

When we have made a new manipulator of say 1/100 scale then the cycle begins again and a new 1/100 scale workshop can be constructed, and so on.

It is entertaining to consider some of the consequences of working with small scale machines. If they are automatic the rate of output of parts should be inversely proportional to the scale. If the machines are made of the same materials they should wear out correspondingly faster, but produce the same number of parts as a big machine would before becoming worn out.

However the weight of a machine of one tenth the linear dimensions, is only one thousandth of that of the bigger model. The material costs become therefore trivial by comparison. Machine tools made from diamonds and precious metals become a possibility therefore, and desirable in that wear and corrosion could be largely eliminated.

At each further stage the amount of space required goes down, and after the first stage is negligible. How many stages can we expect to go down? There seems to me to be an obvious answer. That we can expect most mechanical things to work much as they do on a large scale until the presence of a single atom constitutes a lump on the surface.

It is reasonable to say that most machines work with a tolerance of around 25 microns. I do not expect real trouble therefore until tolerances of say 2.5 Å are required. That is some 10^5 times smaller. Lubrication may become difficult a little before then.

We shall of course have to face Van der Waals forces becoming of major importance, but still they should be small compared with the strength of the materials. We shall also have to be prepared to find our choice of materials at these sizes very limited compared to those on our own scale. The oxide layers we rely upon to protect many of our materials would be as thick as the entire part of the small machine. The strength of materials can be expected to be very dependent on previous history, and new techniques will doubtless have to be found. But at least there is at present as much reason to expert properties to be better rather than worse, as to expect them the other way round. I am told also that diamond tools can be made at present that look sharp even under an electron microscope. These chould take us a good way along our road.

Assuming then that we can make machines some 10^5 times smaller than present ones, is that the end of the road? I don't think so. In fact I think it is at this stage that it really begins to become interesting.

We shall probably at this stage have to avoid all sliding parts, and rely instead on elastic deformation. None the less I think it should be possible to make articles of considerable complexity, even though we shall be working blind.

Let us digress a moment to concern ourselves with the problem of seeing what we are doing. At the first stage of 1/10 we need a binocular microscope of long focal length, say 10 to 15 cm. This has to be capable of being moved around to follow what we are doing. It must be foot or head operated for position and focus to leave our hands free. Even with this however we have become like old men with no accommodation, needing trifocal spectacles. We have very limited depth of focus and are liable to lose whatever we incautiously put down. We can still see reasonably well what we look at directly.

At the next stage our short-sightedness is much worse and we can no longer resolve surface finishes and fine details of any kind, or tell whether our tools are sharp.

At the 1/1000 stage with optical microscopy we are practically blind, and have to work more by feel than sight unless we can call on the electron microscope. There does not seem, at least until we have tried, to be any compelling reason why this should lead to special difficulty, apart from the further limitation on the materials we can employ. All volatile materials have now to be avoided. But the expense, and the trouble of working in vacuum, will put a great premium on learning to work as a blind man does. Perhaps indeed we shall find that the people who shine at such work will in fact all be blind, and have already learned long since the best methods of working without sight. It is conceivable also that it may be feasible to make a kind of feeling camera which could portray a projection of outline at different contours on a cathode ray screen. But this is not the kind of problem we should spend time on now.

But at the last stages even the electron microscope cannot help us.

We need to make a hand, or at least two fingers and a thumb, reasonably slender, and ending at the fingertip in a single atom. Perhaps these should be of diamond. I have no idea at present how they could be made. We need also to be able to measure the position and the force exerted by the fingers, the position to 1/10 of an Ångstrom and the force to about 10^{-6} dynes.

If we have such a machine we shall be able to feel and identify individual molecules. There is good reason to believe that measurements of such fineness and delicacy can be made by mechanical means. The only disturbing forces to be feared would seem to be Brownian motion, the thermal energy of the atoms. Even at room temperature these are only about 1/40 of an electron volt, At 3° K they would be one hundred times smaller. Disturbances of the order 1/40 EV are of course not enough to damage any substance stable at room temperature, or indeed it would not be stable. Any substance to be found in a living cell would be expected to be stable at 3° K.

If we compare this with the electron microscope, the method currently best able to give us fine detail in a non-repeating structure, the comparision is overwhelmingly in favour of mechanical methods. The electron microscope uses electrons with an energy of 50 kv. This is enough to knock hundreds of molecules to pieces. Only the very largest molecules, containing thousands of atoms can be seen.

There is only one compelling thing to be said in favour of the electron microscope. You can buy a model which works well from any of a dozen manufacturers. No one can give you a delivery date for a mechanical molecule feeler, but it may be half a century ahead.

This should not however dissuade us from thinking about it. The detection of the fine movements, say 1/10 Å, with the required small forces should be readily possible by pneumatic means. A valve 10^{-6} cm in diameter with a lid lifting an extra 1/10 Å should admit an extra 100,000 atoms per sec of Helium at 3° K and 1 atmosphere pressure. This is an amount of gas that can be detected by existing vacuum technique. Presumably long before we can make this valve or apparatus we shall be able to detect a small fraction of this. The force exerted by the gas on the lid of the valve would be of the order of 10^{-6} dynes.

I believe pneumatic methods to be far more sensitive than electric or magnetic methods.

With two such hands it should be possible to pick up a molecule and count and identify the individual atoms, and deduce the existence of multiple bonds or ionised groups. No doubt, it could only be done after a lot of practice with known substances had been obtained.

One naturally asks the question whether there is anything in what I have suggested that is forbidden by the uncertainty principle or other known properties of matter. I believe there is not. I should expect to find by these methods precisely the same dimensions, for more or less rigid molecules, as are found by X-ray crystal structure analysis, and for non-rigid molecules, or molecules in a different conformation, essentially predictable results. I do not believe I have overlooked anything to make these speculations impossible. I do not think that the situation that the molecule being examined is in, is in any way peculiar or unusual, except that by clumsy handling reactions might take place which would be characteristic of those occurring at ultra-high pressures, or high temperatures or rates of shear.

It should therefore be possible to take a living cell and freeze it and take it to pieces molecule by molecule. Though this might well be a lifetime's work even with automatic aids, it could scarcely fail to tell us incomparably more than we shall know by that time by other methods.

Other possible uses may appeal more to other people. At every one of the seven or eight stages on the way to this goal new possibilities will open up, so that though I fear I shall not live to see its completion I am confident of some fascinating exercises on the way.

A new pico, as distinct from micro chemistry, should open up very soon. A bacterium, in spite of its mass of perhaps 10^{-12} grammes can synthesise a greater variety of chemical substances than mankind can in his laboratories. We are held back from chemistry on this scale chiefly by lack of suitable apparatus and means to use it, but hundreds of other applications will occur to you as you consider the possibilities.

You may be interested to know that for 3 years I was unable to find any support to carry out these ideas in England, but that Philips have decided to support the first stage of this work. Shortly after I had agreed with Philips, I found that the Royal Society would also have been willing to support me.

In conclusion, I would like to tender my thanks to Her Majesty the Queen of the Netherlands for her gracious approval of my appointment.

Further, I wish to take this opportunity to thank the President and Governors of the "Stichting Eindhovens Hogeschoolfonds" for appointing me professor of this university. I am indebted to the Board of Trustees for their recommendation, and especially grateful for the latitude that permits me to be professor here, in spite of my residence abroad.

My thanks are due also to the members of the Senate with whom I look forward to cooperation in the various fields in which I can be useful. I have had on several occasions the privilege of meeting my colleagues of the chemical department, to which I am attached. I hope that my contacts may soon extend to other departments as well.

Finally, I thank Professor Keulemans, who was the prime mover in the effort that brought me here.

A last word to the student. I shall not be giving a course of lectures on chemistry. I see my function as a consultative one, endeavouring to help with a variety of problems which people bring to me. Above all, I hope that in the course of time, some of you may wish to do research under my guidance.

Ik probeer Nederlands te leren. U zult, als ik een paar zinnen heb gesproken, begrijpen waarom ik toch mijn rede in het Engels heb uitgesproken. Maar graag wil ik in het Nederlands - ook al is mijn Nederlands moeilijk te verstaan - mijn dank betuigen voor de eer die mij ten deel is gevallen door mijn benoeming tot bijzonder hoogleraar.

Ik heb gezegd.