echo soundings are measurements of time, accurate information concerning the units and corrections applied and the type, scale and ultimate accuracy of the recorder used is essential if soundings obtained from various sources are to be combined.

We used as the basic source information for our digital library the soundings on the master plotting sheets for deep sea soundings maintained by the US Naval Oceanographic Office, the Lamont Geological Observatory, the hydrographic departments of the United Kingdom, South Africa, Australia, New Zealand, the Netherlands and Germany.

Each sounding line was inspected for completeness and accuracy of position and depth, and assigned a rating based on general quality. Precision depth measurements accurate to 1 standard unit (t_e), located by methods accurate to better than 1 nautical mile and recorded on charts with a spacing between soundings of no more than 2 miles, were given the highest rank. Soundings of unknown origin, scattered soundings, and soundings of known origin where accuracy was less than 100 t_e or spacing more than 15 miles were in general not included in the library.

Soundings were recorded on punched cards with semi-automatic instruments known as x-y co-ordinate digitizers with a precision for recording co-ordinates of 0·001 in. In this procedure, the recording head was set over the sounding to be read from the plotting sheet. Its depth value was punched by operating a keyboard and its co-ordinates were recorded automatically. The whole process is subject to human error, so verification is imperative. To do this all digitizations were done twice, preferably by two different operators. The two sets of digitized data were then checked one against the other for agreement within predetermined limits of tolerance. This procedure has the advantage that the verification can be done completely automatically on an electronic computer. Initially we used an IBM 7094 computer and later an IBM System 360 Model 75.

For a quick check on position errors, the tracks were plotted either at a reduced scale or at the original scale, and inspected for errors (Fig. 1). By examining computer-plotted vertical profiles gross discrepancies and inconsistencies were eliminated. Position plots and profiles of the digitized tracks were generated with the aid of a cathode ray tube plotter (s-c 4020). This device, peripheral to the computer, reads computer-generated magnetic tape from which it produces the plots and depth profiles on 7·5 × 7·5 in. frames. Position plots and vertical profiles of all tracks are incorporated in the bathymetric library.

The results of the recording, after verification and corrections, are stored on magnetic tape. For each sounding, the following data are recorded: (1) Co-ordinates—latitude and longitude. (2) Sounding (as recorded on source sheet) and units (t_e, fm, m, etc.). (3) Source sheet number. (4) Source track documentation number. (5) Source country. (6) Reliability rating.

We use an auxiliary programme for applying or removing corrections for the velocity of sound according to Matthews's tables[5].

The library now includes over 1 million points from more than 8,000 track segments originally plotted on more than 2,000 source sheets. For every individual sounding-track segment a location plot is included in the library, as well as lists of co-ordinates, depth values, and pertinent source and technical data for each sounding. Vertical profiles have been prepared at an exaggeration of 100:1 for more than 2 million miles of sounding tracks (Fig. 2).

Such a large library necessitates an extensive index. Sounding tracks have been compiled for more than 700 plotting areas according to the US Naval Oceanographic Office numbering system. The library includes lists of all tracks for each area as well as complete listings of source information, including original scales, serial numbers and dates entered. Data from the expeditions of the Lamont Geological Observatory and the US National Science Foundation's research vessel USNS Eltanin are continuously fed into the library. Since 1966, all soundings data acquired by the US Naval Oceanographic Office have been routinely digitized with a system compatible with our library, and survey ships have recently begun collecting bathymetric data in digital form. This new information can be quickly incorporated by machine with data already in the library.

The data library will now be used to construct a new average ocean depth model for use in tidal studies and other global applications. It has already provided plots and profiles for deep sea physiographic studies and will be employed in further quantitative studies of submarine topography.

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The Making of a Scientist

by

H. A. KREBS

Scientists are not so much born as made by those who teach them research, which argues for the perpetuation of centres of excellence. This was the theme of this address by Sir Hans Krebs at the inauguration of the Department of Biochemistry at the University of Newcastle upon Tyne earlier this year.

I BECAME interested in my subject because students have asked me from time to time: "How does one become a Nobel laureate?". I have never before attempted to answer this question because I felt unable to offer an impromptu comment, but when the same question repeated itself I began to reflect on possible answers.

First, I must criticize the question as not being quite appropriate. What is appropriate is the related question :

"How can distinction, or excellence, be attained in science ?". Nobel awards are to some measure a matter of good luck, because their number is too small to do justice to all who would merit an award. A methodical way of finding an answer to the modified question is to study the history and characteristics of scientists of distinction. For this purpose I need a convenient criterion of distinction and, despite what I have just said (and despite some personal embarrassment), I will use the Nobel award as a mark of distinction, for want of a better criterion.

If I ask myself how it came about that one day I found myself in Stockholm, I have not the slightest doubt that I owe this good fortune to the circumstance that I had an outstanding teacher at the critical stage of my scientific career, when from my twenty-fifth to my twenty-ninth year I was associated with Otto Warburg in Berlin. He set an example in the methods and quality of first-rate research. Without him I am sure I would never have reached those standards which are a prerequisite for being considered by the Nobel Committees. I will say a few words later on what in particular I feel I learned from him, but before doing this I would like to examine to what extent the importance of an outstanding teacher applies to other Nobel laureates.

Warburg himself was a Nobel laureate in 1931. He received the prize for his work on the chemical nature of a key enzyme in the reactions between molecular oxygen and foodstuffs in cellular respiration. I was lucky to witness this work from the closest quarters and to take a subsidiary part in it. What were the origins of Warburg's standards ? In an autobiographical note[1] which he wrote in 1964, he remarked that: "the most important event in the career of a young scientist is the personal contact with the great scientists of his time. Such an event happened to me in my life when Emil Fischer accepted me in 1903 as a co-worker in protein chemistry. During the following three years I met Fischer almost daily and prepared, under his guidance, the first optically active peptides". So Warburg's experience and views are very much the same as my own. Let me follow up the story further.

Emil Fischer, Warburg's teacher, was one of the most outstanding chemists of his time. He was awarded a Nobel Prize in 1902 for his work on the chemical structure of sugars, the first of his long series of great achievements. Fischer in turn was a pupil and prolonged associate of another Nobel laureate, Adolf von Baeyer, who received the Nobel Prize after Fischer in 1905, for his discoveries in the field of the chemistry of dyestuffs, in particular for the synthesis of indigo.

Teachers

Since Nobel awards began only in 1901 this criterion of excellence cannot be used for the assessment of excellence in the nineteenth century, but the scientific "genealogy" of earlier teachers and pupils in Fig. 1 shows that von Baeyer was a pupil of Kekulé (famous for his contributions to the structure of organic compounds, especially the ring structure of benzene), and that Kekulé was a pupil of Liebig (who laid the foundation of organic chemistry). Evidently there was also an association with very distinguished teachers in the earlier generations of scientists; had Nobel awards existed in their time, Liebig and Kekulé would certainly have been laureates.

Liebig has provided his own testimony on the importance of a great teacher. He was a pupil of the French chemist Gay-Lussac, the discoverer of some of the fundamental laws of the behaviour of gases. At the time of Gay-Lussac and the young Liebig, Paris was the centre of Continental science and of Continental chemistry in particular. Liebig worked under him in Paris and referred to this experience[2] in the following terms. "The course of my whole life was determined by the fact that Gay-Lussac accepted me in his laboratory as a collaborator and pupil." This is almost the same wording as that of Warburg, written 100 years later. Gay-Lussac was in turn a product of the great French school of chemists, including in particular Berthollet, who pioneered in the concepts of combustion (abandoning the phlogiston theory in favour of the role of oxygen) and elucidated the chemistry of chlorine, ammonia and hydrocyanic acid. One of Berthollet's teachers was Lavoisier.

In every case the association between teacher and pupil was close and prolonged, extending to the mature stage of the pupil, to what we would now call postgraduate and postdoctoral levels. It was not merely a matter of attending a course of lectures but of researching together over a period of years.

Genealogy

So my scientific "genealogy" as summarized in Fig. 1 drives home the point that, in many instances, distinction breeds distinction or, in other words, distinction develops if nurtured by distinction. This is further borne out very forcibly by a consideration of a more extended family tree of scientists. Fig. 2, derived from a chart exhibited in the Munich Museum of Science and Technology (Deutsches Museum), summarizes the genealogy of the Nobel laureates descended from von Baeyer, the pupil of Liebig, and this includes seventeen names. Outstanding discoveries can be associated with all the names. A fuller chart[3], beginning two generations earlier with Liebig, contains more than 60 exceptionally distinguished names and includes more than 30 Nobel laureates.

Seeing this kind of agglomeration of laureates within a scientific family, the sceptic might well suspect a bias in favour of giving prizes to pupils of laureates. In short, does nepotism play a part in the awards ? I hope everybody will agree that the answer to this question is an emphatic "No". The high standing, in the eyes of the world, of Nobel awards is derived from the general recognition of the absolute integrity of the Nobel Committees, and from the knowledge that these committees take a tremendous amount of trouble in finding the most worthy persons.

What, then, is it in particular that can be learned from teachers of special distinction ? Above all, what they teach is a high standard of research. We measure everything, including ourselves, by comparisons; and in the absence of someone with outstanding ability there is a risk that we easily come to believe that we are excellent and much better than the next man. Mediocre people may appear big to themselves (and to others) if they are surrounded by small circumstances. By the same token, big people feel dwarfed in the company of giants, and this is a most useful feeling. So what the giants of science teach us is to see ourselves modestly and not to overrate ourselves. This is a general point.

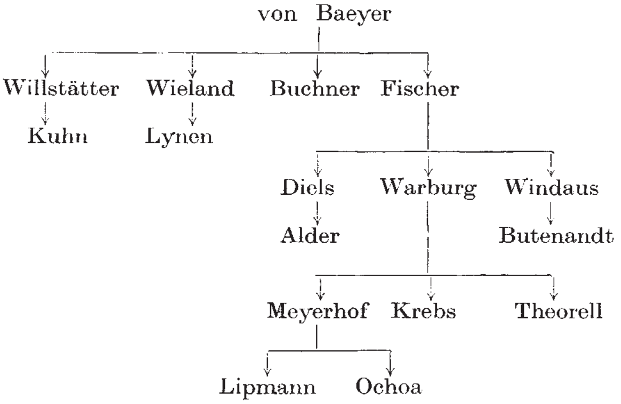
Let me now try to be more specific and quote what individuals have themselves thought about the influence of their teachers. Warburg[1] in his autobiographical

Fig. 1. SCIENTIFIC GENEALOGY

Berthollet	1748–1822
↓	
Gay-Lussac	1778–1850
↓	
Liebig	1803–1873
↓	
Kekulé	1829–1896
↓	
von Baeyer	1835–1917
↓	
E. Fischer	1852–1919
↓	
Warburg	1883 (born)
↓	
Krebs	1900 (born)

Fig. 2. GENEALOGY OF THE VON BAEYER "FAMILY"

The arrows indicate the teacher–pupil link. All members of this "family" are Nobel laureates



note summarized this with reference to his association with Emil Fischer: "I learned that the scientist must have the courage to attack the great unsolved problems of his time and that solutions can usually be forced by carrying out innumerable experiments without much critical hesitation." If I try to summarize what I learned in particular from Warburg I would say he was to me an example of asking the right kind of question, of forging new tools for tackling the chosen problems, of being ruthless in self-criticism and of taking pains in verifying facts, of expressing results and ideas clearly and concisely and of altogether focusing his life on true values. An earlier witness on this question of what one learns from an outstanding teacher was Kekulé who, in 1890, when he was 61, remarked that above all he learned from his teacher Liebig the habit of hard work. He related[4] that Liebig had told him, "If you wish to be a chemist you must be willing to work so hard as to ruin your health. He who is not prepared to do this will not get far in chemistry nowadays". Kekulé added, "For many years four, or sometimes even three, hours of sleep were enough for me". Kekulé, of course, went a bit too far, quite a lot too far, but I do think there is a great deal of truth in attaching importance to the capacity for very hard work.

Opportunities

A recent witness on this question of what distinguished teaching can convey is Jacques Monod[5], who received a Nobel Prize in 1965. In his Nobel Lecture he commented on the importance to him of a Rockefeller Fellowship which gave him the opportunity to work at the California Institute of Technology in the laboratory of Morgan. He describes the influence which the contact with the distinguished people meant to his development as a scientist: "This was a revelation to me—a revelation of what a group of scientists could be like when engaged in creative activity, and sharing it in constant exchange of ideas, bold speculations and strong criticisms: it was a revelation of personalities of great stature such as George Beadle, Sterling Emerson, Bridges, Sturtevant, Jack Schultz and Ephrussi, all of whom were then working in Morgan's Department." Morgan was at that time a Nobel laureate and Beadle became one later.

There is one more witness I want to quote in connexion with the special qualities of what leaders in a subject can teach. This is Otto Loewi, who was a Nobel laureate in 1936, a pharmacologist and physiologist. He said this about the leading physiologists of the nineteenth century and their influence on their pupils[6]: "They shared to the highest degree the qualities of contagious enthusiasm, broadmindedness and imagination, humility and deep devotion to their pupils. These are qualities which in themselves suffice to attract outstanding students. . . . Besides the art of experimenting and observing, the pupils learned the ways of thinking required by science. They learned how to select the object to be explored, how to interpret and evaluate the results obtained, and how to integrate them into the whole body of knowledge. In this way students were not only made familiar with methods and facts, but were imbued with the general scientific spirit which shapes the pattern of the true scholar and investigator."

So, above all, attitudes rather than knowledge are conveyed by the distinguished teacher. Technical skills can be learned from many teachers and, like a modicum of intelligence, are, of course, prerequisites for successful research. What is critical is the use of skills, how to assess their potentialities and their limitations; how to improve, to rejuvenate, to supplement them. But perhaps the most important element of attitude is humility, because from it flows a self-critical mind and the continuous effort to learn and to improve. Also of great importance is the enthusiasm conveyed from teacher to pupil: it is the root of a large capacity for work; it makes the research worker look on research not as work but as a hobby and it also induces him to say "No" when he is faced with tempting diversions leading him to the "corridors of power" or travel on innumerable trips abroad.

Question

I have referred to the importance of asking the right kind of question in choosing a research problem, avoiding those which may give a quick result and concentrating on those which are really worth while tackling. Paul Weiss[7] remarked: "The primary aim of research must not just be more facts and more facts, but more facts of strategic value". By strategic value he meant that an observation or an experiment should lead to the clarification of a problem or deeper insight into a phenomenon, or to the linking of previously unrelated facts and ideas. Goethe[8] expressed the same idea much earlier: "Progress in research is much hindered because people concern themselves with that which is not worth knowing, and that which cannot be known". Medawar[9] has recently stated very succinctly: "If politics is the art of the possible, science is the art of the soluble". How to select worthwhile soluble problems and how to create the tools required to achieve a solution is something that scientists learn from the great figures in science rather than from books.

I would like to underline, on the basis of my own experience, what Monod said about the importance of belonging to a group of scientists such as he found in the California Institute of Technology. Association with a leading teacher almost automatically brings about close association with outstanding contemporaries of the pupil because great teachers tend to attract good people. Students at all levels learn as much from their fellow students as from their seniors and this was certainly true in my own case. Warburg's laboratory at Dahlem, where I served my apprenticeship, was surrounded by other centres of distinction. It was in the same building as Meyerhof's laboratory and the contacts between the two biochemical groups were very close. My own contemporaries included many young people who later became outstanding scientists. There were Ochoa and Lipmann, who became Nobel laureates. There was Lohmann, who discovered ATP and the structure of cocarboxylase; there was Karl Meyer, who discovered hyaluronic acid; there were Hans Gaffron, David Nachmansohn, Dean Burk, Frank Schmitt, Ralph Gerard and Hermann Blaschko. Among the numerous other outstanding scientists working within a few hundred yards, and getting together regularly at the weekly colloquia, were Neuberg, Hahn, Meitner, Haber, Polanyi and Bonhoeffer.

There are many other examples of such centres of excellence and breeding grounds of scientists. Cambridge, for example, was a centre of excellence in physiology and biochemistry in the early decades of this century because Foster, Langley, Hopkins, Barcroft and Adrian were each surrounded by a group of enthusiastic young people of great ability. Cambridge, of course, at the same time was also a centre of excellence in physics, thanks to J. J. Thomson and Rutherford.

No doubt Cambridge and Oxford owe some of their special standing to their size, which made it possible to assemble broadly based groups in a single subject at a time when provincial universities were usually restricted to very small departments with little scope for the cross-fertilization which occurs in the larger groups. It is gratifying to see the recent developments in the provincial universities which have removed this restriction and go a long way in providing a first rate environment.

What I have said so far is not merely a matter of historical reflexions. There are lessons to be learned, in particular by policy makers in the universities who aim at making universities into centres of excellence. As excellence in research is one of the main ultimate roots of all academic excellence, including that of undergraduate teaching, universities ought to do everything in their power to create opportunities for first rate research work by their staff. But do they ? Or, being willing, are they given the means, in terms of facilities and cash, to do so ?

Leadership

In the course of this century there have been only two *really* fundamental advances in the sciences: the first was in the field of atomic physics, leading to the creation of quantum mechanics and the release of atomic energy. The second was in biology where the fusion of biochemistry, biophysics and genetics to form molecular biology has led to an understanding of basic biological phenomena which, only a generation ago, seemed beyond the reach of science altogether. When we compare the circumstances which led to these two great advances we find, as Max Delbrück[10] has pointed out, remarkable differences in the manner in which they have been achieved. Atomic physics was created almost exclusively within the framework of traditional university institutions, whereas in biology the modern developments have not come from the traditional departments of biology. They are largely the results of the efforts of chemists, physicists and biologists, who frequently worked in non-biology departments, and outside the universities. In Britain, decisive advances associated with the names of Wilkins, Crick, Watson, Perutz and Kendrew were made in the Medical Research Council units in London at King's College and at Cambridge, and both these units, financed by the Medical Research Council, were placed in physics and not in biology laboratories. In France, the decisive contributions associated with the names of Lwoff, Monod and Jacob came from the Pasteur Institute, an institution not controlled by a university. In the United States the Rockefeller Institute was a major contributor, through the work of Avery, MacLeod and McCarty, to the new developments. It is indeed most remarkable that universities allowed the initiative in advancing the frontiers of knowledge to slip out of their hands in this way.

The loss of leadership in science by the universities is also borne out by statistics of the Nobel awards to British scientists, which are shown in Table 1. Out of 18 British awards since 1950, only 10 laureates have earned their awards when holding university appointments—and at least one of them, myself, had a privileged appointment with very light teaching and administrative duties at the critical time. The statistics become even more telling when they are limited to the more recent times. Since 1960 only three Nobel awards went to the universities in Britain and five to non-university scientists (and this includes the physical sciences). In this table "other centres" means, in every case except one, the Medical Research Council's units. The exception is A. L. Hodgkin at Cambridge who holds a full-time research professorship of the Royal Society. In comparing these figures one has to bear in mind that the financial resources of the universities are very much greater, as a whole, than those of the Medical Research Council or the Royal Society. The funds at the disposal of the Medical Research Council were rather less than 5 per cent of those available to the universities, and universities employ probably more than 10 times as many scientists as the Medical Research Council. In spite of this handicap the Medical Research Council has a much larger share in the number of Nobel laureates.

Table 1. BRITISH NOBEL AWARDS SINCE 1950

Universities (10)		Other centres (8)	
C. F. Powell	(1950)	A. J. P. Martin	(1952)
J. D. Cockcroft	(1951)	R. L. M. Synge	(1952)
E. T. S. Walton	(1951)	F. Sanger	(1958)
H. A. Krebs	(1953)	F. M. Perutz	(1962)
M. Born	(1954)	J. C. Kendrew	(1962)
C. N. Hinshelwood	(1956)	F. H. C. Crick	(1962)
A. R. Todd	(1957)	M. H. F. Wilkins	(1962)
P. B. Medawar	(1960)	A. L. Hodgkin	(1963)
A. F. Huxley	(1963)		
D. C. Hodgkin	(1964)		

Another illustration of this trend is provided by the statistics of the Fellowship of the Royal Society. Of 32 Fellows elected in March 1967, only 13 did their decisive work in the universities and some of these 13 were again in privileged positions within the university, occupying research posts without teaching commitments.

Why then have the universities lost their leading position in research ? I believe the answer is simple. There is plenty of potential talent in British universities to achieve distinction in science; what is lacking is simply time. Real research of a fundamental character requires a tremendous amount of time. It cannot be done at odd spare moments, nor can it be delegated to technicians or PhD students. The trouble is that senior and junior academic staff tend to be grossly overloaded with teaching, administration and college administration—in particular at Oxford. This overloading often begins at a very early stage of the academic career and leaves junior people insufficient time to mature during the postdoctoral stage. What scientists need for maturing are, I think, several postdoctoral years of essentially full-time research before they embark on teaching on a major scale.

Policies

Another illustration of the importance of time for establishing academic standing is the relatively large number of university professors supplied by Medical Research Council establishments. Between 1961 and 1966, no fewer than 42 Medical Research Council staff went to universities to take up professorial appointments. This was possible because the Medical Research Council provides opportunities that universities cannot provide, giving scientists, above all, enough time. Thus Medical Research Council establishments have proved to be very effective breeding grounds for scientists suitable for senior university posts. I ought to emphasize that it is quite wrong to blame the Medical Research Council (as has been done) for keeping some excellent people away from the universities, when these people, after maturing, return to the universities well prepared for senior appointments.

Research, unlike routine jobs such as teaching or doctoring or administration, needs a minimum critical effort to be effective, and this minimum is very demanding in time. I have often heard it said by those university people who do not know what scientific research means, "Well, if you only have half the amount of time you feel you ought to have, cut down your research by half. What does it matter ?"

This reasoning is false. It is like the idea that in order to cut down the noise of an aeroplane engine the speed of the engine should be reduced. Up to a limited point, of course, this works and the aircraft just travels more slowly. But soon there comes a point when it will no longer remain airborne. At low engine speed it can still taxi along the ground, but that is all.

Scientific research requires a high minimum critical momentum. Effectiveness in research is not just proportional to the effort. The scientist who has insufficient time may manage to taxi along over well ploughed grounds but he will have the greatest difficulty in becoming airborne—doing something really new and original. On the other hand, once he has gathered momentum he will soon find himself in new and unknown territory. One of the most effective ways of attaining a powerful momentum is belonging to a team. Contrary to what some may feel, membership of a team does not at all imply loss of individual scope, of individual initiative, of individual achievement, of individual recognition. What the team provides is a background of aggregate skill, experience and help. This background forms the starting point for individual enterprise.

In the last resort, then, the reason for failing to obtain excellence, in spite of great potentialities, is in many cases the circumstance that those responsible for the organization of the lives of scientists rob them of time.

All this leads to the large question of whether our universities today do as much as they ought to in providing centres of excellence in science, a matter taken for granted a generation ago. In many American universities this is a frequent subject for discussion, and it is perhaps significant that the present United States Secretary for Health, Education and Welfare, John Gardner[11] (formerly President of the Carnegie Foundation for the Advancement of Teaching), has written a provocative book called *Excellence* with the sub-title "Can we be equal and excellent too ?". I am not at all sure whether our main financial sponsors, the University Grants Committee and in particular the Treasury, give sufficient thought and money to the importance of cultivating excellence in the universities; to the fact that in science, teaching and research always go together and that in this age of science the cultivation of excellence in science is not an academic exercise but a source of economic and political strength.

My own apprehensions are naturally influenced by my personal experience at Oxford where, under the banner of equality and democracy, circumstances operate powerfully against the development of excellence in science. In quite a few spheres of the life of this country I fear we have too much equality and too little promotion of excellence. At Oxford very few of the excellent young scientists are given a chance to develop their potentialities in scientific research, merely because they are deprived of the time. A large number of promising and distinguished scientists have for these reasons left Oxford or refused appointments there. This might benefit other British universities if they can show themselves more sympathetic or able to help them, but lack of opportunities, especially in terms of time, has also contributed towards the "brain drain".

Unless we in the universities are aware of these problems and continuously strive for the maintenance of high standards, we are bound to deteriorate. This is a matter of general concern to university people.

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Structure of N-terminal Fragments of Fibrinogen and Specificity of Thrombin

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Determination of the amino-acid sequences of N-terminal fragments from human fibrinogen A and B chains shows that this region of the molecule is highly cross-linked with disulphide bridges and suggests why the proteolytic action of thrombin is so highly specific.

THE fibrinogen molecule is built up from three peptide chains, A, B and C (refs. 1–9). The molecular weight of 340,000 determined for the protein[10] is for a dimeric form of the molecule. The formation of fibrin threads is preceded by a limited proteolysis of the fibrinogen molecule, resulting in the release of fibrinopeptides A and B, respectively, from the N-terminal end of the A- and B-chain of fibrinogen[11–14]. The enzyme causing this limited proteolysis is thrombin. In its proteolytic action on fibrinogen thrombin has a narrow specificity of action. On synthetic substrates of low molecular weight, on the other hand, its action closely resembles trypsin; for example, it cleaves compounds like tosylarginine methyl ester[15]. When acting on fibrinogen only a few bonds are rapidly hydrolysed. These are the arginyl–glycine bonds linking the fibrinopeptides to the rest of the fibrinogen molecule. Some other arginyl and possibly also lysyl bonds in fibrinogen may be split by the enzyme, but apparently at a much slower rate (compare ref. 16).

It has been suggested that the fibrinopeptides might contain structural features which are partially responsible for the narrow specificity of the enzyme[8,16–20]. Structures which might favour a rapid association between enzyme or substrate (or possibly activate the enzyme) are present in the C-terminal part of fibrinopeptide A (refs. 16, 17 and 20). This idea has mainly arisen from the fact that the C-terminal part of fibrinopeptide A has been essentially unchanged during mammalian evolution. Furthermore, it has been shown that fibrinopeptides inhibit thrombin action[13,17]. It should also be mentioned that when cross-