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ACKNOWLEDGEMENTS. I thank Dr M. A. Borbhuiya for his assistance in drawing the figure.

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COMMENTARY

Can great discoveries be orchestrated?

S. Ramaseshan

Many science administrators of India and also Directors of many Institutes have often wondered whether it will be possible to orchestrate great discoveries from this country. It may be relevant to give a few paragraphs from an essay written by Max Perutz, one of the most outstanding scientists of this century.

'Every now and then I receive visits from earnest men and women armed with questionnaires and tape recorders who want to find out what made the Laboratory of Molecular Biology in Cambridge (where I work) so remarkably creative. They come from the social sciences and seek their Holy Grail in interdisciplinary organization. I feel tempted to draw their attention to 15th century Florence with a population of less than 50,000, from which emerged Leonardo, Michelangelo, Raphael, Ghiberti, Brunelleschi, Alberti, and other great artists. Had my questioners investigated whether the rulers of Florence had created an interdisciplinary organization of painters, sculptors, architects, and poets to bring to life this flowering of great art? Or had they found out how the 19th century municipality of Paris had planned Impressionism, so as to produce Renoir, Cézanne, Monet, Manet, Toulouse-Lautrec, and Seurat? My questions are not as absurd as they seem, because creativity in science, as in the arts, cannot be organized. It arises spontaneously from individual talent. Well-run laboratories can foster it, but hierarchical organization, inflexible, bureaucratic rules, and mountains of futile paperwork can kill it. Discoveries cannot be planned; they pop up, like Puck, in unexpected corners.

'In the past, most scientists were poorly paid; only few became famous and even fewer rich. One of the characters in Fred Hoyle's novel *The Black Cloud* remarks that scientists are always wrong, yet they always go on. What makes them continue? Often it is addiction to puzzle-solving and ambition to be recognized by their peers.

'Science has changed the world, but the scientists who changed it rarely foresaw the revolutions to which their research would lead. Oswald Avery never set out to discover what genes are made of; Hahn and Meitner never intended to split the uranium nucleus; Watson and Crick were taken by surprise when their atomic model of DNA told them how the genetic information replicates itself; and when Jean Weigle and Werner Arber wondered why a bacterial virus infected one strain of coli bacteria and not another, they could not foresee that some 40 years on, their enquiry would lead to the cloning of a sheep named Dolly. Like children out on a treasure hunt, scientists don't know what they will find.

'According to Paul Ehrlich, the father of immunology, scientists need the four Gs: Geschick, Geduld, Geld, und Glück (skill, patience, money, and luck). Patience may or may not reap its own reward. The astronomer Fritz Zwicky built a new kind of 18-inch telescope at Mount Palomar in California in order to obtain images over a wide field of the sky. He wanted to scan these images for exploding stars, supernovae which flare up suddenly and can be brighter than a million suns. Between September 1936 and May 1937, Zwicky took 300 photographs in which he scanned between 5000 and 10,000 nebular images for new stars. This led him to the discovery of one supernova, revealing the final dramatic moment in the death of a star. Zwicky could say, like Ferdinand in *The Tempest* when he had to hew wood:

> For some sports are painful and the labour
> Delight in them sets off; some kinds of baseness
> Are nobly undergone, and most poor matters
> Point to rich ends. This my mean task
> Would be as heavy to me as odious; but
> The mistress which I serve quickens what's dead
> And makes my labours pleasures.

'The heavens were Zwicky's mistress, and mine was hemoglobin, the protein of the red blood cells. As part of my attempt to solve its structure, I took several hundred X-ray diffraction pictures of hemoglobin crystals, each taking two hours exposure. I took some of the pictures during World War II, when I had to spend nights in the laboratory in order to extinguish incendiary bombs in the event of a German air raid. I used these nights to get up every two hours, turn my crystal by a few degrees, develop the exposed films and insert a new packs of films into the cassette. When all the photographs had been taken, the real labour only began. Each of them contained several hundred little black spots whose degree of blackness I had to measure by eye, one by one. After six years of this labour, when the data were finally complete, a London firm processed

them with a prehistoric, mechanical punched card computer that produced an output of thousands of numbers. These numbers outlined not a picture of the structure I was trying to solve, but a mathematical abstraction of it: the directions and lengths of all the 25 million lines between the 5000 atoms in the hemoglobin molecule radiating from a common origin. I scanned the maps eagerly for interpretable features and was elated when they seemed to tell me that the molecule consists simply of bundles of parallel chains of atoms spaced apart at equal intervals.

'Shortly after my results appeared in print, a new graduate student joined me. As his first job, he performed a calculation which proved that no more than a small fraction of the hemoglobin molecule was made up of the bundles of parallel chains that I had persuaded myself to see, and that my results, the fruits of years of tedious labour, provided no other clue to its structure. It was a heartbreaking instance of patience wasted, an ever-present risk in scientific research. That graduate student was Francis Crick, later famous for his part in the solution of the structure of DNA.'

However, I must mention that in a very fine and perceptive lecture at the Annual Meeting of the Indian Academy of Sciences (1998), in Kottayam, T. V. Ramakrishnan pointed out that something worthwhile will come from our laboratories only if adequate funds (the 3rd G of the formula given by Paul Ehrlich, i.e. Geld – money) are provided to competent groups in the country. In this connection, I am tempted to tell the story which Lawrence Bragg related to me when he visited Madras. When Max Perutz had taken the X-ray photographs of haemoglobin crystals, Lawrence Bragg went to the Chairman of the Medical Research Council and asked him whether the Council would fund the Cavendish Lab to an extent of 1 million pounds over a period of 5 or 10 years to undertake the crystal structures of molecules of biological interest. In reply to the question asked by the Chairman of MRC, 'What will we get for it?', Lawrence Bragg replied 'one or two Nobel Prizes'. In fact, this investment resulted in 5 Nobel Prizes.

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SCIENTIFIC CORRESPONDENCE

An analysis of the stability of Wien bridge oscillator and a novel way of studying nonlinear devices

A Wien bridge oscillator[1–4] is a resistance–capacitance (RC) oscillator which is widely used for the generation of audiofrequency sine waves over a wide range of frequencies. In this paper, we have tried to find a relationship which relates the output voltage of the oscillator to the different resistances and the parameters of the nonlinear device used for stabilization of the output. This analysis shows a way to study nonlinear devices like semiconductor diodes using AC which is complementary to the standard method of studying these devices using DC. The analysis also shows that if we use a nonlinear device like a tunnel diode which has a more complicated forward characteristic for the stabilization of the oscillator, the device may be driven to a very interesting bistable situation.

An oscillator is a device by which we convert DC input to AC of a suitable frequency. A Wien bridge oscillator shown in Figure 1 is an oscillator whose frequency is given by $1/2\pi\,(RR'CC')^{1/2}$. Let the peak output voltage of the operational amplifier (op-amp 741C) be V. This voltage is fed back to the input of the amplifier via the RC combination. Components of several frequencies are present in the output when the DC power is switched on, but only the component resonant with the frequency given by the RC combination is fed back in the same phase as the output and consequently it is the only component that survives after the transients have died out. The feed back voltage is $V/3$. Two identical diodes in opposition (D_1 and D_2) are used to stabilize the output of the oscillator. The two diodes are active in the two halves of the sinusoidal output. We assume the reverse current through the diodes to be negligible. If the diodes and the R_1, R_3 combination produce an effective resistance $2R_2$, then the gain of the non-inverting op-amp is 3. So the loop gain is unity and all the so-called Barkhausen conditions are satisfied, making sustained oscillation possible. We are interested in finding the output voltage of the oscillator in terms of the different resistors in the circuit and the diode voltage drop.

If the steady state peak output voltage is V, then $2V/3$ must be the drop across R_1, and the same voltage drops across the diodes and R_3 combination. The rest, $V/3$, drops across R_2. If the current through R_2 is I and through R_1 is I_1 we have

$$I = \frac{V}{3R_2}, \tag{1}$$

and

$$\frac{2V}{3} = V_d + I_d R_3 = I_1 R_1, \tag{2}$$

where I_d and V_d are the peak current and peak voltage drop across the diode when the peak output voltage is V. We have worked at low frequencies of the order of a few hundred Hertz. In this region, the output voltage does not depend on the frequency and there is no phase lag between the output and the diode voltage

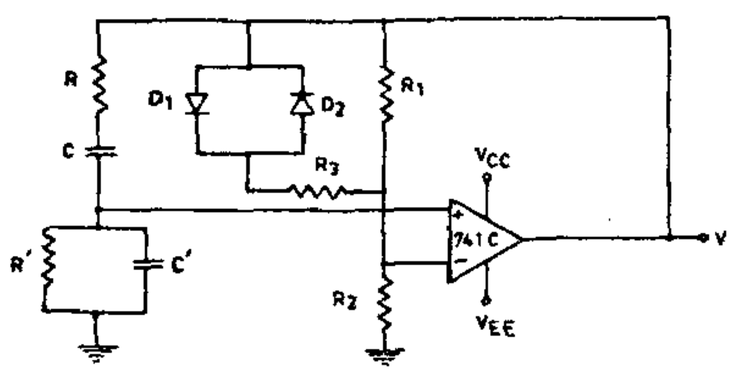

Figure 1. Circuit diagram of the Wien bridge oscillator.