leaching with thermophilic organisms occurs much more rapidly than with mesophilic organisms. However, they also indicate that there are considerable problems in the use of thermophilic organisms for leaching of metals in a practical situation because little is known about the factors necessary for encouraging the growth and development of these organisms.

Conclusion

Although biotechnological applications of thermophiles seem promising, there is no extensive large-scale use. Many thermophiles have only been discovered recently, and extensive research on thermophily has not been carried out. It seems almost certain that something of real value may eventually develop. To date, the most useful process involves the use of a thermostable xylose isomerase for the production of high-fructose syrup for the soft-drink industry. This enzyme, however, has been obtained from a moderate thermophilic microorganism incapable of growing at the temperature at which the enzyme functions. Thus, if a suitable screening method were developed for detecting the production of glucose isomerase, it might be possible to find such enzymes from more typical thermophiles. It should be emphasized that the industrial potential of microorganisms has not yet been realized primarily because the requisite biotechnological research is far from complete.

References and Notes

1. T. D. Brock, *Science* **158**, 1012 (1967).
2. _____, *Thermophilic Microorganisms and Life at High Temperatures* (Springer Verlag, New York, 1978), pp. 303–335.
3. K. O. Stetter *et al.*, *Syst. Appl. Microbiol.* **4**, 535 (1983).
4. J. B. Corliss *et al.*, *Science* **203**, 1073 (1979); F. N. Spiess *et al.*, *ibid.* **207**, 1421 (1980).
5. R. H. White, *Nature (London)* **310**, 430 (1984).
6. H. D. L. Bernhardt *et al.*, *Naturwissenschaften* **71**, 581 (1984).
7. The report of bacteria growing at temperatures of 250°C [J. H. Baross and J. D. Deming, *Nature (London)* **303**, 423 (1983)] probably has an artifactual basis [J. D. Trent *et al.*, *ibid.* **307**, 737 (1984)].
8. M. R. Tansey and T. D. Brock, *Proc. Natl. Acad. Sci. U.S.A.* **69**, 2426 (1972).
9. R. W. Castenholz, *Bacteriol. Rev.* **33**, 476 (1969).
10. _____, *J. Phycol.* **5**, 360 (1969).
11. T. D. Brock and M. L. Brock, *N.Z. J. Mar. Freshwater Res.* **5**, 233 (1971).
12. G. E. Fox *et al.*, *Science* **209**, 457 (1980); C. R. Woese and R. S. Wolfe, *Archaebacteria* (Academic Press, New York, 1985).
13. T. A. Langworthy *et al.*, in *Strategies of Microbial Life in Extreme Environments*, M. Shilo, Ed. (Dahlem Konferenzen, Berlin, 1979), pp. 489–502.
14. M. G. Grütter *et al.*, *Nature (London)* **277**, 667 (1979).
15. M. F. Perutz, *Science* **201**, 1187 (1978).
16. K. Yutani *et al.*, *Nature (London)* **267**, 274 (1977).
17. M. Matsumura *et al.*, *J. Bacteriol.* **160**, 413 (1984).
18. T. Oshima, in *Thermophiles: General, Molecular, and Applied Microbiology*, T. D. Brock and J. G. Zeikus, Eds. (Wiley, New York, in press).
19. T. Imanaka and S. Aiba. *ibid.*
20. An intron was also found recently in the thymidylate synthase gene of bacteriophage T4 in *E. coli* [F. K. Chu *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **81**, 3049 (1984)].
21. B. Sonnleitner, *Adv. Biochem. Eng./Biotechnol.* **28**, 70 (1984); J. G. Zeikus, *Enzyme Microbiol. Technol.* **1**, 243 (1979); P. Weimer, in *Thermophiles: General, Molecular, and Applied Microbiology*, T. D. Brock and J. G. Zeikus, Eds. (Wiley, New York, in press).
22. R. Lamed and J. G. Zeikus, *Biochem. J.* **195**, 183 (1981).
23. S. Zinder, in *Thermophiles: General, Molecular and Applied Microbiology*, T. D. Brock and J. G. Zeikus, Eds. (Wiley, New York, in press).
24. J. Brierley and C. Brierley, *ibid.*
25. D. Claus, P. Lack, B. Neu, Eds., *Catalog of Strains* (German Collection of Microorganisms, Göttingen, Federal Republic of Germany, 1983, and supplement 1984).
26. The preparation of this article was supported in part by a research grant from the National Science Foundation.

What Makes a Good Computer Device?

Robert W. Keyes

The realization of the large digital computer in the 1940's began a continuing search for devices that are better than those in existing machines. The invention of the transistor quickly led to a revolution in digital device technology. Germanium transistors were used in the earliest transistorized computers, but were soon supplanted by silicon devices and silicon transistors embodied in silicon integrated circuits. The integrated silicon chip has been remarkably successful. Increasing integration has rapidly reduced the cost and power dissipation of modern microelectronics and endowed it with high reliability and high speed of operation.

Nevertheless, suggestions continue for alternative computer devices judged to be in some way superior to silicon transistors. Indeed, ever since the introduction of the transistor, major research and development efforts to find a better device have persisted. These efforts have, however, been notably unsuccessful. It behooves us, therefore, to try to identify the reasons for the remarkable achievements of silicon transistor technology and for the failure of the alternatives. Some of the reasons are rooted in chemistry and material science, but others are to be found in the nature of digital computation.

General Purpose Computers

The word "computer" is used here to mean "general purpose computer." Some of the important features that distinguish the general purpose computer are as follows. It can accept many types of problems. The nature and length of the input that defines the problem is not fixed or known in advance. Nor is the length of the calculation known very well; it is often determined by application of a test within the computation to decide if the calculation is finished. In fact, there may be many branch points, at each of which the direction to be taken depends on the results obtained up to that point, embedded in a procedure. Frequent references to random locations in memory must be possible. The computer is constructed from individual logic circuits or gates, entities that perform elementary functions.

Great depth in the handling of information may be involved; that is, the result of an elementary operation is used in a succeeding operation, the result is used again, and so on, through thousands or even millions of steps. For example, in simulating the evolution of a system through time the outputs are recycled to become inputs many times. Information must not be allowed to deteriorate during such long series of operations.

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Digital Representation of Information

The abacus serves as a prototype digital device. Adding another column to the device increases the accuracy of calculation by a factor of 10. This is the advantage conveyed by digital representation: practically arbitrary accuracy is attainable by increasing the number of digits.

Although one uses the abacus for decimal arithmetic, the representation of information is actually binary; there are two possible positions for each bead. Binary representation allows switching between the two states simply and reliably by pushing a bead in one direction or the other. The positions of a bead that represent information are fixed by the bars that retain the wires; the positions are standardized for each digit and the desired position is established over a wide range of force. The binary nature of the representation allows easy setting to a standard position. Binary notation is prevalent in electronic computers for essentially the same reason: it is easy to differentiate between two states with a switch that may be either closed or open.

It is just this ability to refer to a standard that can prevent the deterioration of information during a long series of operations. Even if the representation of a digit is not perfect, if it can still be recognized it can be restored to its standard value (*1*).

The two states in a binary physical representation of information may be designated as 0 and 1. Logic gates, then, perform Boolean operations on the 1's and 0's. The two-input NOR function (Table 1) is an example of the functions that are utilized in computers.

The NOR function illustrates several necessary properties of logic gates: they receive and operate on inputs from several sources. The connection of several inputs to a logic gate is known as fan-in. Similarly, the output of a logic gate must be able to provide fan-out, the furnishing of inputs to a multiplicity of input terminals. Furthermore, the outputs must be isolated from the inputs so that the calculation proceeds in a predetermined direction. Thus, for example, no information as to whether the output of the NOR gate is a 1 or a 0 should be fed back to input A.

A complete set of logic functions must include inversion, that is, the conversion of a 1 to a 0 and vice versa. It is apparent that a logic gate that implements the NOR function can perform inversion (if A = 0 the output is the inverse of B). In fact, it is known that all Boolean operations can be implemented with combinations of NOR gates.

The Large System Environment

Computers contain many logic gates, several thousand in the simplest microcomputers to perhaps a million in the largest systems. Economic feasibility requires that the cost per component be very low. The power consumed per component must be low to contain the heat produced within the limits that can be removed from the system and, in the case of very large systems, from the building in which the system is housed.

Summary. Numerous development projects aimed at replacing the silicon technology that dominates computer logic with a faster alternative have been conducted throughout the past 25 years. None has succeeded. The alternatives are usually based on a device that switches very rapidly, and they neglect many other requirements of computer logic. In this article the essential physical factors that account for the success of transistors in digital applications are identified, as are the factors that are absent in proposed alternative devices.

And the reliability of each element of the system must be very high; large logic systems fail if a single part is inoperative.

Silicon microelectronics has met the objective of low cost through mass fabrication methods, the methods of integrated circuitry. A great many devices are fabricated simultaneously in a series of operations on a large silicon wafer. Low cost precludes the devotion of much effort to any single device. Devices cannot be tested, adjusted, or repaired; they must be used as manufactured. Thus, a lack of high precision of device characteristics must be expected and accepted. I will often refer to this quality, the ability of circuits to operate in the presence of variable device characteristics, in the succeeding text.

The FET Inverter

Transistors have been remarkably successful in meeting the requirements for logic devices in the large system environment. The widely used field-effect transistor (FET) NOR circuit is shown in Fig. 1 (*2*). The active transistors, those that receive the inputs on their gates, are of the enhancement type, that is, they are nonconductive when their gates are connected to ground, and a positive input voltage turns them on by attracting electrons to the surface and establishing a connection between the contact regions known as source and drain (*3*). The load transistor, the transistor in series with the active transistors, is of the depletion type, that is, it is conductive when its gate is connected to its source; in the present case the gate is wired to

the source and the transistor acts as a nonlinear resistor. Thus, when all inputs, V_i, are zero (ground potential), the output, V_O, is connected to the power supply through the resistive FET and is close to the voltage of the power supply, V_B. If at least one of the inputs is positive, it connects the output to ground potential through the active FET and V_O is nearly zero. The output voltage levels are set by V_B and ground, not by the device. This is, indeed, what binary means: there are two standard signal

levels in the system, one of which will be recognized as 1 and the other as 0. Even if the input signal has been degraded 10 or 20 percent by, for example, series resistance in wires or electrically induced voltages, the output is restored to its intended value. The operation of the circuit is shown in Fig. 2a in the form of a load line on the FET characteristics; Fig. 2b presents the result as a curve of output as a function of input.

The high gain of the input-output characteristic makes the standardization of the output possible. High gain means that a small change in the input near the threshold at which the FET becomes conductive effects a large change in the output. Large voltage ranges, called noise margins, on either side of the threshold are provided in which the output has one of the standard values. The threshold can vary, as shown by the dotted line in Fig. 2b, and not destroy the operability of the circuit. Therefore, the necessity for high precision in the fabrication of the devices is relieved. This point must be emphasized: the high gain of the device allows the circuit to operate in the computer environment, where great precision and reproducibility of device characteristics cannot be achieved.

There are other features that account for the ability of the FET NOR to function so successfully in computers. Some of these may seem trivial or obvious, but the lack of just such qualities plays a role in the failure of novel technologies to provide even working hardware, much less systems that can compete with those based on transistors.

The gate is not sensitive to the condi-

tion of the output; there is good isolation of input from output. Both charge and voltage can be amplified. Current can flow through the transistors for a long enough time to charge or discharge a large number of following stages; excellent fan-out capability is provided. The circuit as drawn in Fig. 1 shows how fan-in is accepted. Voltage can be amplified, at least to the extent that a degraded input signal can be restored to the standard value. The circuit can switch in either direction in comparable amounts of time, so no separate resetting operation is needed. And the inversion that is necessary for a complete logic system is available.

Variability in Devices

One might wonder if the variability of characteristics in logic devices might simply be avoided and the construction of digital logic systems thereby greatly simplified. While there is no fundamental reason why this cannot be achieved, each source of variability is rather formidable.

Perfect control of processing parameters cannot be achieved. Any variability in the temperature of a reaction or an annealing step, the concentration of a reagent, or the intensity of radiation during an exposure appears as variability in the parameters of devices. The problem is not only one of maintaining control of macroscopic tool parameters, reagent purity, cleanliness, and so forth. In mass fabrication all sorts of inhomogeneities—in temperatures, in starting materials, in gas flow patterns, in almost any physical quantity in the processing chamber—are unavoidable.

Furthermore, processes do not attempt to control the exact locations of defects, impurities, and dopants. It is hoped that they will be absent, or, if present, that their effects will be determined by a uniform average. As miniaturization progresses, however, averages involve fewer and fewer defects and dopant atoms, and nonuniformity grows.

Also, devices can and do change with age and use. The irreversible phenomena known as creep, diffusion, bleaching, corrosion, electromigration, and thermomigration cannot be entirely avoided, and they change the properties of device structures. A system must tolerate a certain amount of such changes in devices.

In addition to variability in the physical structure of devices, they are operated in a variety of environments. Temperature is probably the most important

Table 1. Binary logic function NOR.

p	q	p NOR q
0	0	1
0	1	0
1	0	0
1	1	0

environmental variable. Device specifications invariably demand operation throughout a temperature range, and similar ranges are encountered in practice. Practically all physical properties of materials depend on temperature, and such things as Fermi levels, dielectric constants and indices of refraction, and energy gaps are directly reflected in device characteristics. Properties vary rapidly with temperature in the vicinity of resonances and critical points, and the large effects associated with such points are consequently not useful for digital device purposes, even though they may appear attractive at first sight.

Finally, precision is basically incompatible with miniaturization. If a dimension can be controlled to within, say, 0.25 μm, should the manufacturing process be based on nominal 10 μm to obtain high reproducibility or on 1 μm to maximize the number of components per unit of area? Such questions are almost always decided in favor of the smallest dimension consistent with other considerations.

Novel Devices

Some research into novel devices aims only to replace silicon with another semiconductor, and some proposes to use quite different phenomena and device principles. Most is inspired by a quest for speed, based on a hope that a faster device will allow a faster computer to be realized. However, devices must satisfy

Fig. 1. The FET NOR circuit.

many criteria described above if they are to be useful in a large computer. These other aspects of devices are rarely examined in advance. In addition, system speed depends on things other than fast devices. If, for example, the devices are large or dissipate high power, the distances and the transit times of signals between them will be large and system speed degraded.

Various alternative electronic technologies will now be examined. The first two, being transistors, actually share most of the desirable properties of silicon transistors. The differences lie in the areas of material science and semiconductor physics. The specific details of current research interest for the technologies will not be discussed; they could fill many volumes.

Germanium Transistor

Germanium is a superior semiconductor for transistors from the point of view of a physicist or device theorist; its hole and electron mobilities are more than twice those of silicon. Charges move more rapidly, and one hopes for higher speeds of operation. Since the initial replacement of germanium by silicon, there have been intermittent attempts to revive germanium as a higher speed replacement for silicon (4). One of the most important reasons that silicon is favored, however, is not physical but chemical: the oxide of germanium has neither the excellent passivating and dielectric properties nor the great chemical stability of SiO_2. One may still hope that, instead of relying on the native oxide, a film with the required properties could be deposited on the germanium, but such a technique has not yet emerged.

The lower energy gap of germanium compared to silicon is also not favorable to its use in integrated circuitry. The high device density inevitably means that the temperature of the semiconductor will rise above that of the environment. The temperatures found in silicon circuits would excite many electrons across the intrinsic energy gap in germanium and inhibit proper functioning of devices based on p- and n-type materials. Use of germanium transistors in dense integrated systems would entail a much greater investment in cooling than silicon.

Gallium Arsenide MESFET

The other semiconductor that has received serious attention as a competitor for silicon in logic is gallium arsenide (5).
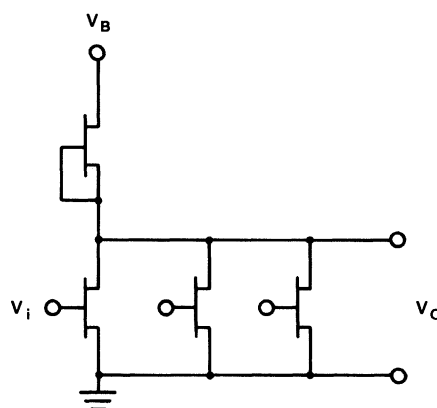
Electrons have higher mobility in GaAs than in silicon or germanium, and GaAs has a higher intrinsic energy gap than silicon, so that intrinsic conductivity is not a problem. However, no insulator comparable to SiO_2 is known for GaAs either, and a quite different kind of device technology has developed that is based on the MESFET (metal-semiconductor field-effect transistor). A thin layer of semiconductor doped to be conductive is formed on a high-resistivity substrate. The potential barrier that is formed at a metal-semiconductor interface is used to deplete the thin conductive layer of electrons (6). The energy gap of GaAs is so large that its intrinsic conductivity can be neglected, and GaAs of very high purity constitutes a substrate of very high resistivity; it is said to be semiinsulating. The high purity required to make intrinsic semiinsulating GaAs is difficult to achieve. However, impurities that form electron states far below the conduction band, so-called deep traps, can be introduced. The energy gap is so large that these deep traps hold electrons even at operating temperatures, allowing semiinsulating GaAs to be made by doping with trapping impurities. The existence of semiinsulating GaAs makes the MESFET a convenient device to use (7, 8).

Metal deposited between source and drain contacts to the conductive layer performs the function of a gate. Application of a negative potential to this gate widens the depleted region and, if the conductive layer is thin enough, depletes it of electrons, cutting off conduction between the source and the drain. The use of the MESFET to perform logic thus is similar to the use of insulated gate field-effect transistors. If the conductive layer is made so thin that the entire layer is depleted in the absence of application of a potential applied to the gate, then the MESFET is "normally off"; it can be turned on by a positive voltage on the gate, which reduces the thickness of the depleted region.

The difficulties of using GaAs MESFET's in logic circuits are rooted in material science. The threshold voltage, the voltage applied to the gate that just depletes the conductive layer, is sensitive to the concentration of dopants in the conductive layer and to the thickness of the layer, both of which must, therefore, be carefully controlled. The solubility of donor impurities in GaAs is smaller than solubilities in silicon, causing difficulties in fabricating low-resistance ohmic contacts. GaAs is chemically less stable than silicon, and processing methods are correspondingly restricted. For ex-
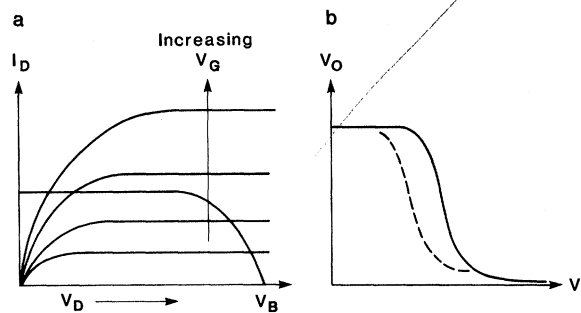
Fig. 2. (a) Operation of the NOR circuit. The output lies at the intersection of the load line and the FET current voltage curve corresponding to the gate voltage applied at the input terminal. (b) Transfer characteristic, V_O versus V_i, of the NOR circuit, which reproduces the course of the voltages at the intersections in (a) in the V_O-V_i space.

ample, lower temperatures must be used to avoid decomposition of GaAs.

The advantage of high mobility in GaAs and other semiconductors is diminished as miniaturization advances because of the phenomenon of velocity saturation. Electron velocity does not increase indefinitely in accord with the mobility as electric fields increase. Rather, the electron energy increases and new electron-scattering mechanisms that limit velocity come into play and limit velocity to some finite value. The differences among the saturation velocities of semiconductors are not as great as the differences in mobilities. Since electric fields increase with reduction in dimensions, velocities approach saturation values and the differences between semiconductors become smaller.

The promise of GaAs first began to be appreciated around 1970, when MESFET's with gate lengths of 1 μm and less were realized (9). These devices had higher maximum frequencies of oscillation than any solid-state device known at that time. They were soon developed as radio frequency amplifiers. Exploitation as logic elements came more slowly, however. In spite of many recent successes of attempts to develop working GaAs integrated circuits, its future as a competitor of silicon is still in doubt, although it may, of course, find its own unique areas for application.

Threshold Logic

Novel technologies, especially those that have no easy way to perform inversion, often propose to use a form of Boolean operation known as threshold logic (10). Simply stated, the idea is that a number of 1 inputs, M, to a logic stage are summed, and if the sum is equal to or greater than some value N then the stage switches. M and N are small integers. A popular example is the multiple-input AND, such as a three-input AND, in which an output is produced only if all three inputs are 1. Although working electrical circuits have been built in this

way and used for computation, the method places great demands on the accuracy of components and signal levels and is not suitable for integrated circuitry.

To illustrate the point, consider that the three-input AND is to be implemented by adding three inputs with a nominal value of 1 V. The threshold for switching is set to a nominal value of 2.5 V, so that two inputs do not excite a response but three do. Assume that the inputs and the threshold might actually be above or below their nominal value by 15 percent (inputs in the range 0.85 to 1.15 V and threshold in the range of 2.2 to 2.8 V). Then three inputs could sum to only 2.55 V and two to 2.3 V; the circuit might not operate properly in the presence of the uncertainty.

Tunnel Diodes

Tunnel diodes were found to switch very rapidly shortly after their discovery and were soon pursued as candidates for digital logic devices. The basic reason for the high speed is that they carry current at high density; a small device can have a large transconductance. They can be made small enough to have only a very low capacitance. The high current then can charge the capacitance in a short time.

A way of performing logic with tunnel diodes is illustrated in Fig. 3 (11). The power supply (shown as a battery) drives current in series through the tunnel diode and a resistor. The state of the circuit is determined by the intersection of the resistive load line with the tunnel diode characteristic (states A and B in Fig. 3b; state C is unstable). A three-input AND is realized as follows: current inputs are fed from preceding stages through resistors P and add to the current supplied through series resistor R. If the sum of all the currents is greater than the peak current of the diode, then the intersection of type A no longer exists and the circuit is forced to switch to state B. The input currents are adjusted so that two will not cause the current to exceed the
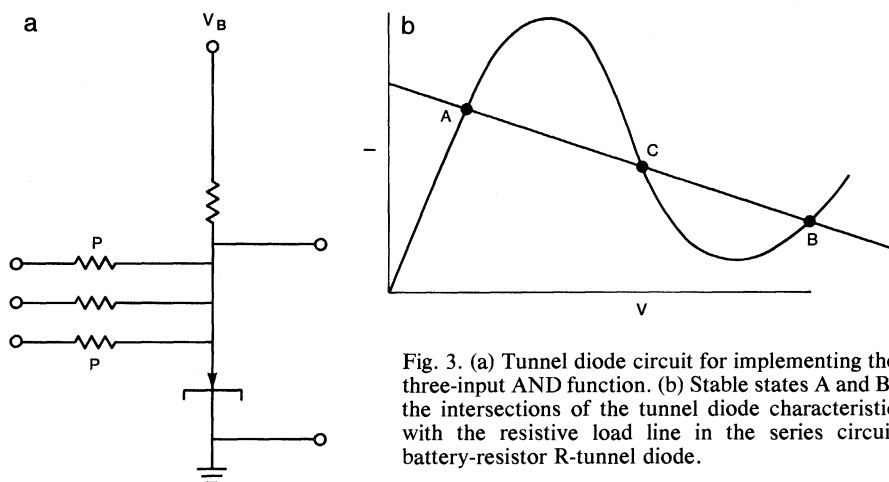
Fig. 3. (a) Tunnel diode circuit for implementing the three-input AND function. (b) Stable states A and B, the intersections of the tunnel diode characteristic with the resistive load line in the series circuit battery-resistor R-tunnel diode.

peak value while three will. The unsuitability of the tunnel diode circuit for digital logic seems clear in light of the previous discussion. It depends on threshold logic, while in fact a reproducibility of the peak current of ± 25 percent was difficult to achieve (12). The input is not well isolated from the output; signals can propagate back through resistors P. Many circuits having additional components to improve isolation were invented. The gain is not large; transformers were sometimes introduced to increase it. The circuit cannot be switched in the opposite direction, from B to A; a separate resetting operation must be provided. Nevertheless, interest in the application of the tunnel diode in computer logic continued well into the 1960's.

Josephson Tunneling

The development of logic devices based on the Josephson effect in superconductors has been pursued in many laboratories during the past decade. Various circuit and device types have been investigated, usually with lead and its alloys and niobium being used as superconductors (13, 14). The basic factor motivating interest in Josephson devices is the low voltages involved in the effect, as compared to the voltage levels of semiconductor devices. The low voltages mean that only small charges are stored on capacitors, and the power is, therefore, very low. The currents can be comparable to those known in other technologies; the small charges then lead to fast switching.

The idea involved in Josephson logic devices is that a tunnel junction can carry a certain amount of current with zero voltage across it. The maximum zero-voltage current depends on applied magnetic fields and on quantum interference effects with other junctions in a multijunction circuit.

I will not describe all the different circuits that have been devised to use the Josephson effect. The limitations of the use of the devices to perform logic in large computers can be explained by consideration of an example, the two junction-interferometer (Fig. 4a). Its operation was succinctly described by Gheewala (15):

A Josephson interferometer logic circuit consists of an interferometer which is biased in the superconducting state by a gate current I_g. The interferometer consists of two Josephson junctions, each with a threshold current I_0 connected in parallel by inductances L. When the interferometer is switched into the voltage state the gate current is transferred into a terminated output transmission line. . . . An electromagnetically coupled control line . . . induce[s] magnetic flux in the interferometer loop. The induced flux modulates the threshold curve of the interferometer as shown by the . . . curve.

The essentials of the curve in question are reproduced in Fig. 4. The continuous line separates the flux-current space into a zero-voltage region and a voltage state region. The switching action is suggested by the dashed arrow terminating at point X in the voltage state. The load can consist of several control leads of other interferometers to permit the output to act as the input to following logic stages with moderate fan-out. Fan-in can be obtained with a multiplicity of control lines in a single interferometer, arranged so that threshold logic can be performed or as an OR gate, where any one input can cause switching by placing several devices in series. The switching times of a circuit are very small and careful attention to matching impedances of devices and interconnections is necessary to prevent degradation of the output current

pulse by reflections from impedance discontinuities.

There is a fundamental limitation in the basic effect that leads to switching: the current being controlled produces a magnetic field which adds to that of the controlling field; the device cannot differentiate the two. The controlled current must, therefore, be of similar magnitude to the controlling current; high gain is not possible. The interferometer is designed to cancel the effect of the biasing current, but perfect cancellation is not likely to be achieved. The absence of high gain requires that the devices be fabricated within close tolerances.

Ideally, a small change in control current should move the operating point from the zero-voltage to the voltage state. The ability of the small charge in control current to switch a much larger bias current to another path constitutes gain. However, there can be substantial uncertainty in the location of the boundary between the two regions. The location of the boundary depends on the characteristics of the Josephson tunnel barrier, the size of the devices, and the mutual inductance between the control line and the current loop. The properties of the tunnel junction may change with time, especially if the chip is subject to frequent heating to room temperatures and cooling to cryogenic temperature. Allowance must also be made for uncertainty in the current that is intended to switch the circuit, as it is determined by devices with similar sources of variability. In addition, thermal noise is appreciable in Josephson circuits because of the small energies involved in the operation of devices. Thus, much variability in the parameters of devices is not permitted. If a large change in control current is required to overcome the uncertainty in the location of the boundary between the voltage and zero-voltage states, the gain is degraded. In fact, a refined fabrication technology is needed to make devices consistently that can be switched at all.

The advantage to be gained from the low energy requirements of Josephson logic must also be viewed in the context of the capacity to remove heat in the liquid helium environment. The energy dissipated in a Josephson switching operation might be 1000 times less than that dissipated in a conventional circuit. However, the density at which heat can be removed from the system is also less. An optimistic estimate of the maximum rate of heat removal in a liquid helium bath is 1 W/cm^2. At least 20 W/cm^2 and probably 100 W/cm^2 will be available in room temperature systems. My thermal

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models (16) suggest that a fourfold increase in speed may be available if a working system can be realized. The question facing Josephson development is thus, is a factor of this magnitude large enough to support development of an entirely new computer technology? Uncertainties about the ultimate success of the technology and the possibility of surprises from more conventional technologies must be taken into account in answering the question.
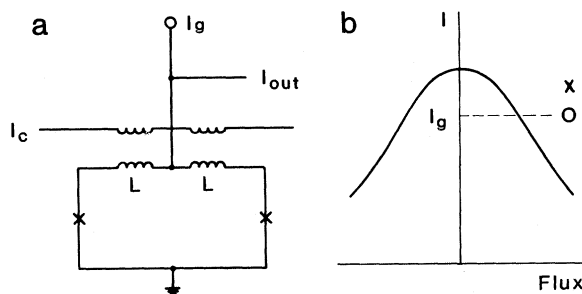
Optical Logic

Bistable or hysteretic effects in lasers and interactions between lasers were observed soon after the discovery of various types of lasers between 1960 and 1962 (17). Proposals for computers based on such effects were formulated (18). There has been little progress toward working elements during the intervening decades, however. Nevertheless, discussion of the subject persists, partly because of the interest of physicists in optical bistability as an intriguing example of chaotic and cooperative phenomena (19).

One must be careful to distinguish between optical logic for a general purpose digital computer, which is the present subject, and optical computing, a large field of endeavor based on the filtering and transformation of images with masks and lenses. Since many bits are necessary to describe an image, the methods can be said to process many bits in parallel. They differ from digital logic in that each information stream follows a predetermined path from light source to final transducer, with no possibility of branching or referring to memory. The length of the process is limited by the lack of any standardization or means for level restoration. A particular physical implementation can perform only one particular set of operations. These methods promise to be useful for a variety of purposes and are the focus of much research and many conferences on optical computing.

Interest in optical logic for general purpose digital computing currently centers on optical bistability. Optical bistability arises from nonlinear effects at high light intensity that change the index of refraction or the absorption constant of a substance. Bistability means that the light transmitted through a body of material may have two values for a certain range of incident intensities under proper conditions. Bistability leads to hysteresis, which means that the trans-

mitted intensity depends on the history of the incident intensity and not just on its current value. In other words, the optical device can be in either of two states, depending on its previous exposure to light. Some form of optical feedback within the device is needed to achieve bistability.

The most common way of providing the necessary feedback is through the use of an interferometer, an optical cavity with reflecting end faces. The number of optical wavelengths in the device determines whether it is in a highly transparent or relatively opaque state. The number of wavelengths depends on the index of refraction, which in turn depends on the intensity of the light. It can be shown that only a few stable optical states correspond to a given incident intensity (19). The idea of optical logic is that a light signal coming from one device can change the state of another device.

It can be seen, however, that such a scheme does not have the desirable properties of digital logic elements. The basic phenomenon bears a certain resemblance to one of the difficulties of Josephson logic, namely, both the controlled signal and the controlling signal produce the same effect, a change in the index of refraction in the present case, so high gain cannot be achieved. The characteristics of an interferometer depend sensitively on the relation of the wavelength of the light to the length of the cavity, and close control of the length and of the index of refraction is required. The output is not standardized to any reference but depends on the inputs and on the device. Means of achieving fan-out to drive many other devices are not apparent; it has been suggested that light amplifiers be added to make fan-out possible. In some experiments the controlling light is of a different wavelength from the controlled light, so that the output is unsuited to influence another device. The controlled cavity is optically coupled to the cavity providing the input, allowing strong interaction between input and output. The proposals for per-

forming elementary logic functions such as AND are implemented in threshold logic with its additional implications for precise control of all system parameters. Laboratory studies demonstrate switching in only one direction. It is not surprising that few attempts to construct even something as simple as a ring oscillator from optical components have been made, although the phenomenon of optical bistability has been known for two decades (17).

Summary

The many fruitless attempts to find a device technology that performs logical operations faster than silicon circuitry may cause one to wonder if there is any simple answer to the question, what makes a fast computer? There probably is no simple answer; there are, however, several essential ingredients that are readily identifiable (20).

A fast computer is more than just a collection of devices that can be separately made to switch rapidly. The devices must work in a system environment; they must be able to influence one another and to do so with fan-out and fan-in. Each must be able to make reliable binary decisions concerning the meaning of signals received. The system environment is unforgiving, devices must be packed closely together to minimize the time taken for signals to propagate between them and to take advantage of the economies of mass fabrication, interconnections must be miniaturized for the same reasons, and there are many opportunities for signals to be degraded by resistance and electrical interactions. Device performance is affected by the heat produced by surrounding devices and is changed by the irreversible effects of strong currents, high light intensity, stress, and temperature gradients. Success in preventing signal deterioration and loss in such an environment has been achieved by establishing reference signal levels throughout a system and resetting the signal level to its correct

Fig. 4. (a) Two-junction Josephson interferometer (15). The X's in the circuit are the Josephson junctions. (b) Division of the current flux plane into two regions.

value at each step. The standardization of a degraded signal at each step requires a response of the type shown in Fig. 2b, which is achieved through the use of devices with high gain.

The most prominent defect in novel devices that have been seriously considered as alternatives is a lack of high gain. No device with the high gain of transistors has appeared in the decades since the replacement of the relay and the vacuum tube by transistors. Without high gain close attention to the reproducibility of component parameters is needed, but such reproducibility is difficult to achieve in dense arrays of miniaturized components.

Other desirable features that have been mentioned should not be forgotten: isolation of input and output, ability to perform inversion and to switch both ways in comparable amounts of time so

that no separate resetting operation is needed, and a potential for attaining the high packing density needed in high-speed systems.

Finally, the barrier to the introduction of new materials into electronic technology increases each year as conventional silicon technology continues to improve.

References and Notes

1. A. W. Lo, *IRE Trans. Electron. Comput.* **10**, 416 (1961).
2. C. Mead and L. Conway, *Introduction to VLSI Systems* (Addison-Wesley, Reading, Mass., 1980), pp. 1–33.
3. S. M. Sze, *Physics of Semiconductor Devices* (Wiley, New York, ed. 2, 1981), chap. 8.
4. F. H. Dill, A. S. Farber, H. N. Yu, *IEEE J. Solid-State Circuits* **3**, 160 (1968).
5. R. van Tuyl and C. Liechti, *IEEE Spectrum* **14**, 41 (March 1977).
6. S. M. Sze (*3*), chap. 6.
7. M. Morkoç and P. M. Solomon, *IEEE Spectrum* **21**, 28 (February 1984).
8. R. Dingle, *IEEE Trans. Electron. Devices* **31**, 1662 (1984).
9. K. Drangeid, R. Sommerhalder, W. Walter, *Electron. Lett.* **6**, 228 (1970).
10. S. L. Hurst, *Threshold Logic* (Mills & Boon, London, 1971).
11. S. P. Gentile, *Basic Theory and Application of Tunnel Diodes* (Van Nostrand Reinhold, Princeton, N.J., 1962), chap. 8, section 3.
12. D. P. Holmes and P. L. Baynton, in *Gallium Arsenide*, A. C. Stickland, Ed. (conference series No. 3, Institute of Physics and the Physical Society, London, 1967), pp. 236–240.
13. H. H. Zappe, in *Advances in Superconductivity*, B. Deaver and J. Ruvalds, Eds. (Plenum, New York, 1983), pp. 51–127.
14. E. J. Vanderveer, in *Large Scale Integrated Circuits Technology*, L. Esaki and G. Soncini, Eds. (Nijhoff, The Hague, 1982), pp. 728–746.
15. T. Gheewala, *Appl. Phys. Lett.* **33**, 781 (1978).
16. R. W. Keyes, *IEEE J. Solid-State Circuits* **15**, 193 (1979).
17. C. J. Koester, R. F. Woodstock, E. Snitzer, *J. Opt. Soc. Am.* **52**, 1323 (1962); A. B. Fowler, *Appl. Phys. Lett.* **3**, 1 (1963); M. I. Nathan, J. C. Marinace, R. F. Rutz, A. E. Michel, G. J. Lasher, *J. Appl. Phys.* **36**, 473 (1965); R. L. Fork, *Appl. Phys. Lett.* **8**, 162 (1966).
18. G. J. Lasher and A. B. Fowler, *IBM J. Res. Dev.* **8**, 471 (1964); W. F. Kosonocky, *IEEE Spectrum* **2**, 183 (March 1965).
19. L. A. Lugiato, *Contemp. Phys.* **24**, 333 (1983); K. Ikeda, *Opt. Commun.* **30**, 257 (1979); K. Ikeda, H. Daido, O. Okimoto, *Phys. Rev. Lett.* **45**, 709 (1980); C. R. Willis, *Phys. Rev. Sect. A* **29**, 774 (1984).
20. R. W. Keyes, *Physics of VLSI* (Addison-Wesley, Reading, Mass., 1985).

Production of 2-Keto-L-Gulonate, an Intermediate in L-Ascorbate Synthesis, by a Genetically Modified *Erwinia herbicola*

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The commercialization of recombinant DNA technology has mainly involved the use of convenient microbial or animal cell hosts for the manufacture of foreign proteins. However, the application of this technology in the chemical industry for the production of small molecules has also begun (*1*). We now report the construction of a recombinant "metabolically engineered" bacterial strain that is able to synthesize 2-keto-L-gulonic acid, a key intermediate in the production of L-ascorbic acid (*2*).

At present, most L-ascorbic acid (vitamin C) is produced by a modification of the Reichstein-Grussner synthesis (*3*, *4*), a lengthy and capital-intensive route that involves a microbial fermentation and a series of chemical steps (Fig. 1). The last intermediate in the Reichstein-Grussner

synthesis (Fig. 1) is 2-keto-L-gulonic acid (2-KLG), a compound that can easily be converted into L-ascorbic acid via a simple acid- or base-catalyzed cyclization (*2*). A number of organisms from the coryneform group of bacteria (*Corynebacterium*, *Brevibacterium*, and *Arthrobacter*) as well as species of *Micrococcus, Staphylococcus, Pseudomonas, Bacillus*, and *Citrobacter* are able to carry out the microbial conversion of 2,5-diketo-D-gluconic acid (2,5-DKG) into 2-KLG (*5*). Furthermore, a number of species of *Acetobacter, Gluconobacter*, and *Erwinia* can efficiently oxidize D-glucose to 2,5-DKG (*5*, *6*). Thus, 2-KLG can be

produced from D-glucose via 2,5-DKG by a cofermentation of appropriate microorganisms from the above two groups (*5*). Sonoyama *et al.* have also published a tandem fermentation process, with the use of mutant strains of *Erwinia* and *Corynebacterium*, for carrying out the glucose to 2-KLG conversion (*7*) (Fig. 2).

Although the tandem fermentation represents a considerable simplification in the route from D-glucose to L-ascorbic acid, our goal was to simplify this process further by combining the relevant traits of both the *Erwinia sp.* and the *Corynebacterium sp.* in a single microorganism. To accomplish this we identified the 2,5-DKG reductase in the *Corynebacterium sp.* (*8*) that was responsible for the conversion of 2,5-DKG into 2-KLG. The gene for this reductase was then cloned and expressed in *Erwinia herbicola*, a bacterium of the family Enterobacteriaceae that is able to convert D-glucose into 2,5-DKG (*8*). The resultant organism is able to convert D-glucose into 2-KLG in a single fermentation (Fig. 2).

Identification, purification, and characterization of the *Corynebacterium sp.* 2,5-DKG reductase. Although the efficient conversion of 2,5-DKG into 2-KLG by whole cells of a *Corynebacterium sp.* mutant strain had been demonstrated (*7*), essentially nothing was known about the

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