Perspectives

Information theory: A guide in the investigation of disease

J A MORRIS

Department of Pathology, Royal Lancaster Infirmary, Ashton Road, Lancaster, LA1 4RP, UK

(Fax, 1524-846346; Email, kay.edward@l.bay-tr.nwest.nhs.uk)

1. Introduction

Information as a precise mathematical concept was a product of the twentieth century (Shannon 1948; Cherry 1957; Green and Swets 1966; Miller 1968). The advent of telecommunications led to a need to measure information. Engineers send information along telegraph or telephone wires and through the ether as radio waves. They need to measure the amount in order to ensure that the systems are efficient. The development of the digital computer also brought the study of information to the forefront of intellectual attention. The second world war acted as a major impetus. Breaking the enigma code was an important contribution to the war effort showing that information was as important and real as tanks and guns and planes. It was shortly after the war in 1948 that Claude Shannon published the mathematical theory of information, one of the intellectual triumphs of the century. In 1952 Watson and Crick showed that DNA was the molecule of information and ushered in the molecular biological revolution. We are now surrounded and dominated by the artefacts of the age of information. Computers, e-mail, the internet, word-processing, e-banking, e-commerce, and mobile phones are products of this fundamental concept of information to which Shannon brought mathematical precision. In this article I intend to explore the extent to which information theory can help in understanding biological processes and in particular can act as a guide in studying disease.

Information is a fundamental concept, like energy, it is difficult to define because it has no component parts but it can be measured. The unit of measurement is the bit and this is defined as the amount of information which reduces uncertainty by one half. Thus if a crime is committed and there are one hundred equally likely suspects there is considerable uncertainty about who is the culprit. If an item of information reduces the number of suspects from one hundred to fifty then this is equivalent to one bit of information. More formally:

Information in bits =

$$\log_2 \frac{\text{The initial number of possibilities}}{\text{The final number of possibilities}}$$

(assuming that all possibilities are equally likely).

Information and uncertainty are closely related ideas and both are essential to the theory of information. Heisenberg's uncertainty principle, published in 1927, revolutionised physics and changed for ever the way we should think about the nature of physical reality. We can no longer assume that a specific cause will lead inevitably to a specific effect. Instead, cause and effect are linked by probability and we can only predict that which is likely to occur not that which will occur. The clockwork universe of Newton with its certainties is replaced by one dominated by uncertainty. This has profound consequences for biology as argued below.

Experimental psychologists were the first group of biological scientists to use information theory (Cherry 1957; Green and Swets 1966; Miller 1968). One important factor was that Alan Turing, who had a major role in the development of the digital computer as well as the breaking of the enigma code, was interested in the workings of the mind. He thought that the mind was a machine and he wanted to produce a machine that could think. It was natural therefore for psychologists to use the new digital computer as a model in studies of the brain. Experimental psychologists did not make the mistake of assuming that digital computers were the same as the brain because in many respects they are not. Instead they argued that digital computers process information and the brain processes information so that the general principles which apply to all information processing systems will apply to both. It was these general principles emerging from the work of Shannon and illustrated by computers which were used to probe human behaviour.

My introduction to information theory came in the late 1960s. In the third year of my undergraduate course in medicine at Cambridge I took an intercalated degree in experimental psychology and information theory was the big idea at that time. Donald Broadbent, head of the experimental psychology unit in Cambridge and a fellow of my own college (Pembroke College) was a leading protagonist. He emphasized the difference between software and hardware, new concepts at that time at least to me, and famously argued that it did not matter whether the brain was made of neurones or rubber bands; the important thing was the logic which drove the system.

A common problem used in information theory at that time, clearly a product of that age, was the decision strategy to use when a man views a radar screen in order to detect an incoming aeroplane. The decision task is to distinguish signal from noise (figure 1). A signal is an intense burst of photons from a small spot on the screen. Noise is due to a low intensity of photons arising from the screen in the absence of a signal. The number of photons for both signal and noise is a random variable and the frequency distribution of signal and noise will overlap. In this detection problem there are two correct responses and two incorrect responses. The two correct responses are to respond 'signal' when signal occurs (correct positive) and to respond 'noise' when noise occurs (correct negative). The incorrect responses are to respond 'signal' when noise occurs (false positive) and to respond 'noise' when signal occurs (false negative). Analysis of this problem reveals that it is not possible to respond correctly with complete certainty, there is always a finite chance of error. It is possible to adopt a strategy which reduces or even eliminates errors of one type but this automatically increases errors of the opposite type. Thus reducing false positives leads to an increase in false negatives and vice versa.

In the radar detection problem, if the strategy is to maximize the number of correct responses, it can be shown that the observer must consider not only the evidence of his eyes, i.e. the number of photons emerging from the screen, but also a priori probability, i.e. the relative likelihood of signal and noise. Thus if noise is much more likely than signal the decision to respond 'signal' will only be made if the intensity is high. The optimum decision strategy, however, is not to seek the maximum number of correct responses but to maximize expected value. To achieve this the observer must also take into consideration the rewards and penalties associated with correct and incorrect responses (utility). In the radar problem a false negative, i.e. failing to detect a signal, could be disastrous if it is an enemy aeroplane. This is an error to avoid. A false positive by comparison is a lesser mistake.

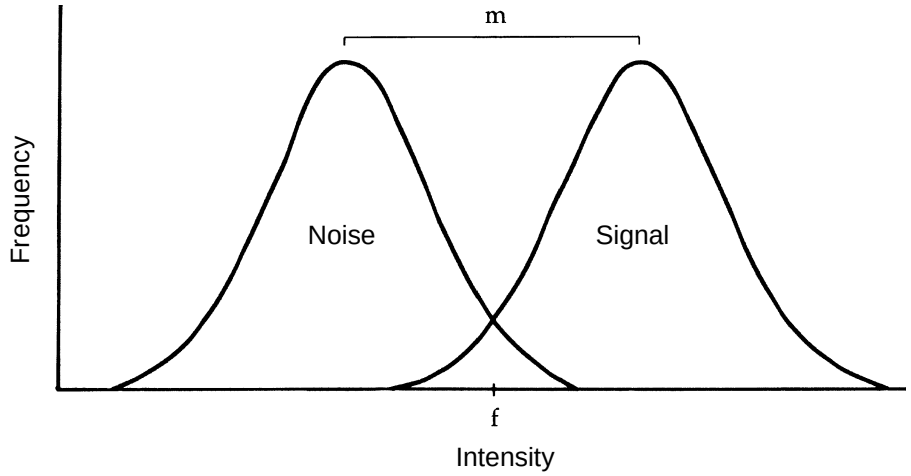

Figure 1. The frequency distribution of the intensity of light arising from a radar screen when a signal of intensity "m" occurs compared with no signal (noise). The decision threshold at "f" means than any intensity greater than "f" is regarded as signal and any intensity less than "f" is regarded as noise. If signal and noise are equally likely a decision threshold placed at "f" would minimize but not eliminate errors. If the a priori probability of noise is greater than signal the decision threshold must be moved to the right to keep errors at a minimum. Moving the threshold to the right increases false negatives but reduces false positives. The optimum decision is to maximize expected value and this depends on a priori probability, the intensity observed (evidence), and the values and costs associated with correct and incorrect decisions.

Decision theory teaches us:

(i) The optimum decision strategy is to maximize expected value.
(ii) An optimum decision depends on a priori probability, evidence and utility.
(iii) There is always a finite chance of error.
(iv) Reduction in errors of one type automatically increases errors of the opposite type.

When I started clinical medicine after my year studying experimental psychology it seemed to me that our biological systems were making vast numbers of decisions every day in the battle to preserve health and fight disease. In this process errors will occur and will contribute to disease. Thus decision theory and information theory should have applications in understanding and investigating disease.

Early studies of information theory used the digital computer as a model and attempted to identify the general principles of information processing which would apply to both the brain and the computer. A neural network is another example of an information processing system, which in many respects is closer to the brain than is the digital computer. I would like to suggest that the immune system is also an information processing system (Morris 1987). In the first few weeks and months of life the human infant meets an enormous number of common bacteria which establish residence on the surface of the respiratory and gastro-intestinal tracts. These bacteria present a vast array of different epitopes to the immune system and there is a decision problem to distinguish shapes that are foreign from shapes that resemble self antigens. Failure to recognize a shape as foreign will increase the risk of infection, failure to recognize that a bacterial epitope is the same as a self-epitope will increase the risk of autoimmune disease (Morris 1987). This detection problem is logically equivalent to the radar detection problem and the general principles of decision theory apply to both.

The idea of information processing in biological systems can be applied more widely. An adult human male is composed of approximately 10^{14} cells, and can be regarded as an individual because these cells act together and therefore function as a single unit. This can only occur because of a flow of information between the cells, often in the form of small molecular messengers (cytokines). Thus the whole of biological activity can be regarded, in some sense, as the product of information flow and the general principles of information processing can be applied to all aspects of biological behaviour.

Some of the general principles that apply to information processing are as follows:

(i) All information processing systems have a finite capacity.
(ii) Information is processed in a background of noise and there is always a finite chance of error.
(iii) The components of a discrete information processing system will decay with time according to the laws of entropy and the probability of error will rise.
(iv) Complex information processing systems use redundancy to reduce error.

In the rest of this article I intend to explore to what extent these general principles can help in the study of disease. To be useful it is obviously important to move from such very general statements to specific testable hypotheses.

2. Information and the microbial flora

The first principle states that there is a limit to the rate at which information can be processed. This limit is likely to be reached when a baby is born and it is suddenly exposed to a vast array of micro-organisms, many of which establish residence on the body surface. The human infant is aided in the process of responding to microbial antigens by maternal IgG transmitted across the placenta and by IgA present in maternal milk. Cows' milk is a poor substitute in terms of immunoglobulin specificity and therefore infants who are not breast fed will be at a disadvantage in terms of responding appropriately to their microbial flora. This leads to the specific prediction that formula fed infants will be at increased risk of infection and of autoimmune disease. The former risk is well known but recently it has been established that breast feeding protects against insulin dependent diabetes mellitus (IDDM) and asthma (Borch-Johnsen *et al* 1984; Alberti 1993; Oddy *et al* 1999). It is possible to produce other explanations of the latter observation such as the suggestion that bovine albumin incites the disordered immune response, but this is post hoc. Information theory leads from general principle to specific prediction which accords with observation. This is much more valuable in scientific terms than a post hoc explanation of the same facts. Information theory, however, goes even further and predicts that epitopes on bacteria of the normal body flora incite the response that leads to the autoimmune disease IDDM and the disordered allergic disease asthma (Morris 1987, 1989). This prediction is contrary to conventional wisdom and only time will show whether or not it is correct. The value of information theory is this power to generate new testable ideas.

The second principle of information theory is also very important. Information is processed in noise and therefore there is always a possibility that errors will occur when decisions are made. Even perfect systems operating optimal decision strategies have a finite chance of making a mistake. This is the biological manifestation of the uncer-

tainty principle. Pathologists tend to assume, probably because they have not come to grips with uncertainty, that if autoimmune disease arises there must be something wrong with the immune system. It must be sub-optimal in some way and the aim of investigation should be to find out what is wrong and attempt to correct it. Decision theory teaches us that perfect systems make mistakes, and even though it is true that imperfect systems will make more mistakes, the approach to investigation is to define the conditions under which the decision is made and then attempt to influence circumstances so that the mistake becomes less likely. The above example of breast feeding protecting against IDDM illustrates this. IgA in milk will combine with bacterial epitopes and lower the rate at which they are presented so that the immune system has more time to respond (in terms of decision theory this allows more evidence to be gathered and analysed).

The third and fourth principles can be combined to give an interesting explanation of ageing. Mistakes increase with age as components decay and disease becomes more common. Redundancy reduces the rate at which mistakes occur and influences the rate at which they increase with time. The effect of redundancy is that errors rise slowly initially and then more rapidly so that there is a long period of good health in early and middle life followed by a rapid decline in old age. Mathematical models based on the third and fourth principles predict a relationship between mortality and age in humans which is very close to that observed in the United Kingdom (figure 2) (Morris 1992). There are of the order of 60000 mutations a second arising in the cells of each individual (these are mutations which have not been repaired). The steady accumulation of these mutations with age will interfere with all aspects of biological capability, cells will be less able to function as a unit, mistakes will be more likely to occur and health will decline. These mutations are in part spontaneous and in part the product of environmental mutagens. If exposure to the latter could be reduced we would live longer and healthier lives.

The third and the fourth principles indicate that errors rise with time and disease increases steadily with age. The interaction of micro-organisms with the immune system is, however, more complicated. Common bacteria and viruses are likely to be met early in life and the probability of a first encounter falls progressively with age. Thus the chance of disease in response to first exposure of any specific organism is a combination of two opposing factors; the probability of first exposure falls with time but the probability of an error on first exposure rises with time (Morris 1987, 1989, 1990). The result is an age incidence curve which rises to a peak in early or middle life then falls (figure 3). The majority of autoimmune diseases show this pattern. For instance multiple sclerosis rises to a peak in the late twenties or early thirties, psoriasis peaks in the late teens and IDDM reaches a peak in the early teens. These age incidence curves can be explained if multiple sclerosis, psoriasis and IDDM are caused by an immunological error at the time of first exposure to some common micro-organism. Using mathematical models it is possible to go further. Figure 3 shows three curves, if we know two of the curves it is possible to calculate the third. Using mortality curves for the rising error function and published curves for disease it is possible to infer that 50% of the population encounter the organism which pre-

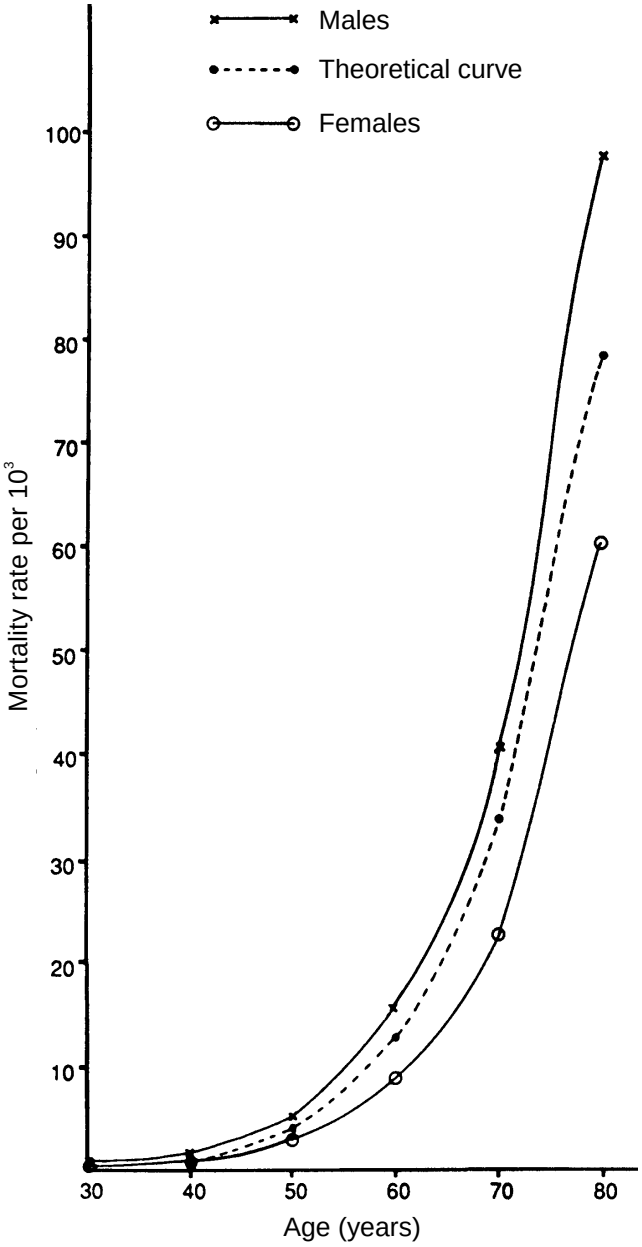

Figure 2. The mortality rates for males and females in England and Wales compared with a theoretical curve based on the information theory model.

cipitates multiple sclerosis in any four year period (Morris 1990). The organism, or organisms, which cause psoriasis are even more common and those causing IDDM are very common indeed. In fact the age incidence curve of IDDM is the age of disease presentation, and since disease onset is much sooner the model leads to the prediction that the causative organisms must be bacteria of the normal body flora rather than viruses (Morris 1989). This is contrary to conventional wisdom but once again illustrates the predictive power of ideas from information theory.

These ideas lead to the concept that the microbial flora presents a vast amount of information to which our bodies need to respond. The rate at which new information is presented is maximal in the first year of life but goes on throughout life. This information flow is a major, and perhaps the major, challenge to our decision systems. Mistakes in the process, which are inevitable, will be a major cause of disease. In my opinion, and only time will tell whether this is right or wrong, the interaction between the microbial flora and the mucosal immune system will be one of the big areas in pathology in the next half century. Bacteria and other micro-organisms can cause disease by invasion of tissue, and this is well documented, but they can also cause disease by the secretion of toxins and by inciting disordered immune responses. A wide range of conditions including sudden infant death syndrome, autism, schizophrenia (Morris 1996), autoimmunity (Morris 1987) and the myriad skin conditions of hitherto unknown cause are probably a direct product of this disease mechanism. Even those sceptical of these claims will agree that this is a line of investigation which should be pursued.

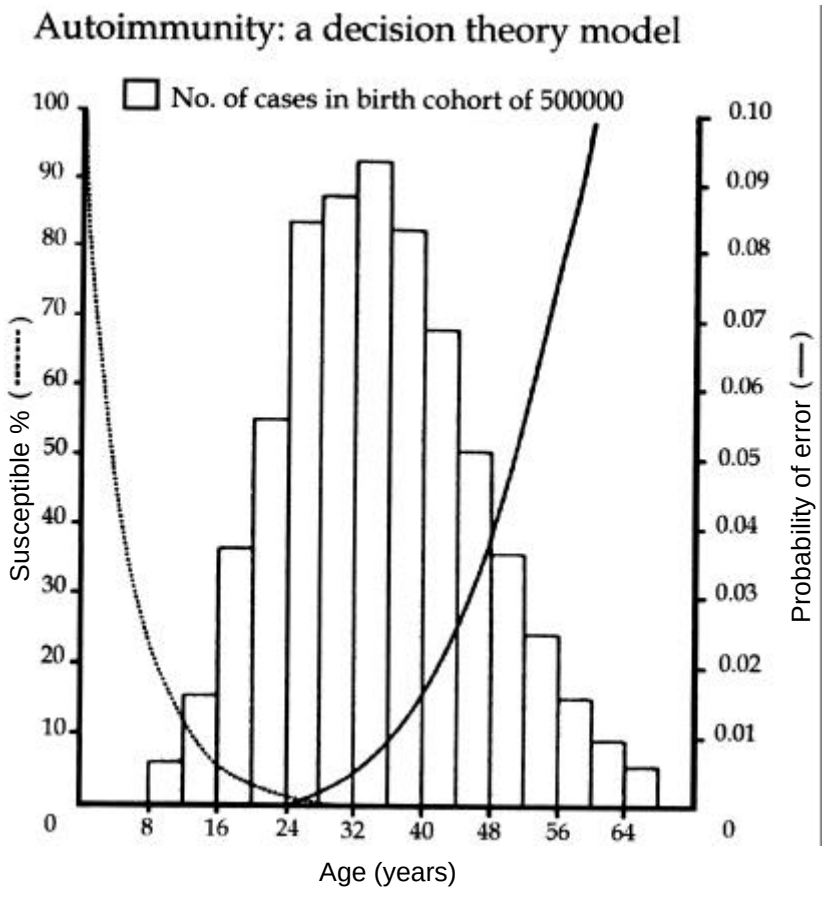

Figure 3. The histogram shows a theoretical incidence for an autoimmune disease which arises when first exposure to a micro-organism leads to an error in immune decision making. The probability of first exposure to a common micro-organism falls rapidly with age but the probability of error rises with age, the resultant disease incidence rises then falls. If the micro-organism is very common the peak of the disease incidence moves to the left. If the organism is less common the peak of disease incidence moves to the right.

3. Genetic control and redundancy

Information theory can also be used to probe the role of genetic control in biological processes. Advanced life forms, such as humans, are complex and the complexity is ultimately specified by information stored in genetic systems. Information theory teaches us that it is impossible to have a functioning effective complex system without a high level of redundancy (Morris 1997). This is because complicated systems have a large number of components, each of which is at risk of error and breakdown. If there is no redundancy a single error or a single component malfunction will lead to failure of the entire system. A high level of redundancy will allow a complex system to continue to function in spite of errors. It is for this reason that redundancy is an essential component of all information processing systems and the higher the level of complexity the higher the level of redundancy required. A consequence of this idea is that genetic codes must specify redundant components, but if that is the case single deleterious mutations in genes will have no significant effect on function and biological fitness. This in turn means that there can be no effective selection against single deleterious mutations and they will accumulate in the genome through successive generations. There must be a limit to this process, of course, or the species would become extinct. An intriguing question is how does selection occur?

As far as we know, evolution has no foresight and redundancy cannot be designed into a complex system in the way that engineers introduce redundancy. The simple, but profound, principle, however, is that a non-redundant, complex system would not work, and therefore functioning complex biological systems must be highly redundant. We do not know how redundancy evolves, but it must in some way arise by chance and be maintained because of a competitive advantage. One can see this is possible in relation to fighting infection. If the probability of dealing effectively with an infection and surviving is 0·9 then another layer of redundancy could increase it to 0·99 and a further layer to 0·999. In each case the absolute increase is small but still a major competitive advantage.

If there were no element of redundancy in the genome it would not puzzle us because we would not be here to be puzzled. The fact that we are capable of posing the question gives us the answer, there must be redundancy in the genome (and the proteome and in physiology).

An important property of redundancy is that deleted components interact synergistically to degrade performance (figure 4). Consider a redundant system in which seven identical components scan a histological slide in order to detect malignant cells. There is a one in ten chance that a single component will miss a particular cell. The probability that all seven components miss the cell is one in ten million. This system would be regarded as very reliable. If only six of the components are in working order the probability of missing the malignant cell would be one in a million. This is still very reliable but ten times less reliable than before. Thus as each component is lost the error rate rises ten-fold and eventually the system would become unreliable. This is illustrated in figure 4. The loss of one or two components in a redundant system might have no noticeable effect but further loss will lead to significant deterioration in performance. In biological systems a small number of deleterious mutations might have little or no effect but a few more will impair fitness and allow selection to occur.

In the six million years since humans and chimpanzees evolved from a common ancestor, deleterious mutations have entered the genome at a rate of approximately four per generation (Eyre-Walker and Keightley 1999). This means each individual has, on average, four mutations in the germ line which were not present in the germ line of either parent (this is the average during human evolution, other evidence suggests it is close to two in Europe today). The estimate of four depends on measuring the rate at which synonymous base substitutions occur in the genetic code and assuming the same rate applies to non synonymous base substitutions. It is assumed that there is no selection against synonymous base substitutions as they do not affect protein structure. This rate of base substitution is then extrapolated to the genome and the rate at which new mutations arise is calculated. There must be some way of selecting against these mutations but mathematical models indicate that this cannot be based on

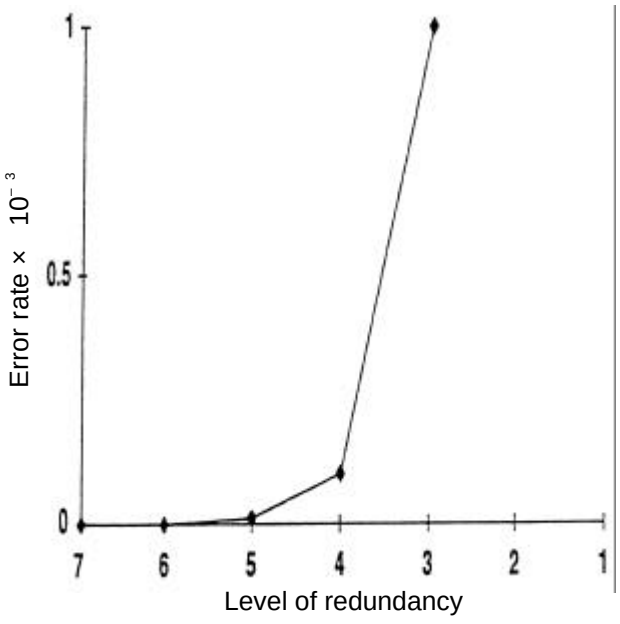

Figure 4. The error rate rises as the level of redundancy is reduced.

dominant or recessive disease (Kondrashov 1994; Redfield 1994). There will be selection against a single deleterious mutation which causes a dominant disease, but this can only apply to a minority of genes if four new mutations arise in each generation. Recessive disease will also select against deleterious mutations and preserve the functioning gene in the population, but calculations show that if most genes were preserved in this way the number of deleterious mutations in the heterozygote state would be high and cousin marriages would be sterile (Morris 2001). In fact the fertility of cousin marriages is not markedly different from that of the general population, this indicates that the overall load of deleterious mutations is relatively low, at least in those genes which cause significant recessive disease.

The third way that selection can act is by polygenic mechanisms, and this is exactly as predicted by the redundancy model. One or two deleterious mutations have little effect on biological function or fitness, but additional mutations in the same system impair performance and there is selection against those individuals. A mathematical model of how this system might work has been published elsewhere (Morris 1997). Let us assume that the human genome contains N separate systems of equal size each containing the same number of genes (mathematical models are always simplifications, obviously the human genome will contain overlapping systems of varying size with varying levels of redundancy). One or two deleterious mutations in a system will have only a small effect, three deleterious mutations will impair function to a significant degree, and four deleterious mutations in one system will prove fatal during the early stages of intrauterine life. This simple model leads to some interesting predictions which have profound consequences for biology.

(i) The majority of advanced organisms reproduce sexually rather than asexually. The model based on deleterious mutations offers a simple but compelling explanation. If an organism reproduces asexually the number of deleterious mutations will increase with each generation and eventually the organism will become extinct ('Muller's ratchet'; also see Kondrashov 1994). In sexual reproduction deleterious mutations are distributed at random to gametes and then gametes fuse at random to form zygotes. The result is that deleterious mutations are distributed unevenly to zygotes, some have more and some have less than average. Those with less than average are more likely to survive and contribute to the next generation. Thus in an organism which reproduces sexually new deleterious mutations arise with each generation, but deleterious mutations are also lost by selection during development and the overall number in the population can remain constant. It is of interest that cloning is a form of asexual reproduction, and the cloned animal will always have at least as many and usually more deleterious mutations in the germ line than the parent. The cloned product will usually be worse, occasionally as good but never better than the parent (Morris 1999a). It is only in sexual reproduction that progeny can have fewer mutations than their parents. Species survive because sexual reproduction is a stochastic process, but survival depends on the generation of inequality.

(ii) The number of deleterious mutations in the genome will influence every aspect of biological performance including the development of physical symmetry, ability at sporting and intellectual tasks, and success at preserving health (Morris 1999b). Consider a very complex robot which is extremely clever in that it can perform a wide range of tasks. The ability to mow the lawn, do the housework and play chess are just a few of its many accomplishments. The robot is specified by a large number of instructions and it has neural networks which allow it to learn from the environment. If we pose the question "which of the instructions makes it clever?", there is no sensible answer. The robot's cleverness is a product of all the instructions and its environment. Consider a series of defective robots in which some of the instructions have been deleted. If the robots are highly redundant the deletions will have varying effects. A small number of deletions might have little noticeable effect, but in general the more deletions that are made the more the abilities of the robots will be impaired. Cleverness will be inversely related to the number of deletions. This will only be a correlation because in some cases a few deletions could have a marked effect whereas in other cases many deletions might have a small effect. Thus in summary if we delete instructions at random from a clever complex system, cleverness will be impaired and the degree of impairment will be correlated with the number of deletions. Furthermore all aspects of complex behaviour will be at risk so that the effect of deletions is all pervasive.

(iii) The ability to fight disease and preserve health depends on multiple complex systems. The model therefore predicts that the risk of polygenic disease will be correlated with the number of deleterious mutations in the genome. Those with the most deleterious mutations will be most likely to develop ischaemic heart disease, maturity-onset diabetes mellitus, hypertension and schizophrenia.

(iv) In any population there will be a balance between the number of new deleterious mutations arising in each generation and the mean number of deleterious mutations in the germ line of individuals. If the rate at which new mutations occur falls the mean number of deleterious mutations in the population will also fall and the entire population will be more healthy, more intelligent and more physically attractive. If the mutation rate rises the converse will occur. In the United Kingdom the health of the population has improved since the industrial revolution and this could be explained if the mutation rate has

fallen. Economic advance provides protection from the environment in the form of better housing, improved sanitation and a year round varied food supply. The latter in particular provides anti-oxidants which can reduce the mutation rate. Industrial societies also pollute and there is a possibility that the mutation rate could rise in the future leading to impairment of health. It is for this reason that a system to monitor mutation rates is required.

4. Application

Information theory is concerned with the software rather than the hardware of disease. It paints a broad picture of the logic of the interaction between the environment and a complex information processing system. Using insights from information we can generate specific hypotheses about disease causation. To prove the hypotheses we need to build models, make predictions and test them using epidemiological data and laboratory experimentation.

Consider the enigmatic disease schizophrenia. The pathogenesis is unknown but there are a few generally accepted facts (Morris 1996).

(i) The disease is a products of genetics and the environment.
(ii) The pattern of inheritance is polygenic rather than dominant or recessive.
(iii) The lifetime prevalence is close to 1% in most communities.
(iv) The age incidence of disease presentation rises to a peak in early adult life and then falls.
(v) Toxic states, such as chronic amphetamine abuse, can mimic the disease.
(vi) There are consistent neuroanatomical abnormalities with atrophy of subcortical grey matter around the third ventricle.

Consider the hypothesis that schizophrenia is due to impairment of function of a large complex genetic system concerned with clearing bacterial toxins from the systemic circulation. Impairment occurs because of the presence of deleterious mutations.

(i) Deleterious mutations in a system increase the chance of failure they do not guarantee failure. The disease will not always occur and environmental factors will influence the probability of occurrence.
(ii) Deleterious mutations lead to a polygenic pattern of inheritance, at least three mutations are required to cause disease.
(iii) Deleterious mutations occur in all communities and the probability of at least three mutations in a large genetic system will be approximately the same in all racial groups. This contrasts with disease caused by one, two or three specific mutations as the prevalence of specific mutations varies markedly between communities.
(iv) If the clearance of bacterial toxins is immune mediated the age incidence of disease will be similar to that shown in figure 3.
(v) A number of bacterial products are neurotransmitters and they could induce a state of acute or chronic toxic psychosis.
(vi) The maximum exposure to new bacterial products coincides with the maximum flow of new information into the developing brain. Damage to the brain by this exposure to toxins is plausible. The pathology of diffuse damage to the subcortical grey matter fits better with bacterial toxins than with tissue invasion by micro-organisms or with autoimmune disease.

The specific predictions that arise from this idea are as follows:

(i) The lifetime prevalence of schizophrenia is close to 1% in all communities. But those communities which have experienced a lower mutation rate due to improved social conditions will have a slightly lower prevalence than communities in which the mutation rate is higher.
(ii) It should be possible to measure circulating bacterial neurotransmitters in patients with acute psychosis.
(iii) Systemic treatment with pooled immunoglobulin should reduce the level of circulating bacterial toxins.

Many readers might regard this as a flight of fancy. The point I wish to make, however, is that information theory can generate specific testable hypotheses. If the hypothesis is wrong it can be tested and shown to be wrong. Karl Popper claimed this was the way that science progressed. The new ideas from information theory are often contrary to common sense, they are certainly contrary to conventional wisdom, for this reason alone they are worth pursuing.

5. Conclusion

The development of disease and the preservation of health can be analysed in terms of both software and hardware. The software approach, based on information theory, allows biologists to narrow down the range of possibilities and frame hypotheses to direct epidemiological and laboratory based research. These ideas follow from the basic principles which apply to all systems that process information: (i) finite capacity, (ii) finite probability of error, (iii) the error rate rises with age and (iv) complex systems need a high level of redundancy.

The vast array of epitopes presented by the microbial flora to the mucosal immune system is one of the major information challenges to our decision systems. Investigation of this interaction will be one of the big areas in biological science in the next half century. A wide range of

hitherto ill-understood diseases are likely to be a consequence of mistakes in this interaction.

Preservation of health, intelligence and physical attractiveness is ultimately dependent on the integrity of the genome. Deleterious mutations in somatic cells lead to ageing and in germ cells they impair the health of future generations. A challenge for pathology is to measure and monitor mutation rates in the general population. If the overall mutation rate could be reduced we would live longer and healthier lives and future generations would be healthier, more intelligent and more attractive.

This conclusion is controversial but I believe I can defend it. The point I make is that physical attraction is like health and intelligence. They are all three products of our genes interacting with the environment. If deleterious mutations are introduced into the genome, all three risk being impaired. This does not mean that other factors are not important, but all three ultimately depend on information held in the genome. If the information is degraded all three will be affected.

References

Alberti K G M 1993 Preventing insulin-dependent diabetes mellitus; *Br. Med. J.* **307** 1435–1436

Borch-Johnsen K, Jone G, Mandrup-Poulsen T, Christy M, Zachau-Christiansen B, Kastrup K and Nerup J 1984 Relation between breast-feeding and incidence rates of insulin-dependent diabetes mellitus; *Lancet* **324** 1083–1086

Cherry C 1957 *On human communication* (Cambridge, Massachusetts: MIT Press)

Eyre-Walker A and Keightley P D 1999 High genomic mutation rates in hominoids; *Nature* (*London*) **397** 344–347

Green D M and Swets J A 1966 *Signal detection theory and psychophysics* (London: John Wiley)

Kondrashov A S 1994 Sex and deleterious mutations; *Nature* (*London*) **369** 99–100

Miller G A 1968 *He psychology of communication* (London: Penguin Press)

Morris J A 1987 Autoimmunity: a decision theory model; *J. Clin. Pathol*. **40** 210–215

Morris J A 1989 A possible role for bacteria in the pathogenesis of insulin dependent diabetes mellitus; *Med. Hypotheses* **29** 231–235

Morris J A 1990 The age incidence of multiple sclerosis: a decision theory model; *Med. Hypotheses* **32** 129–135

Morris J A 1992 Ageing, information and the magical number seven; *Med. Hypotheses* **39** 291–294

Morris J A 1996 Schizophrenia, bacterial toxins and the genetics of redundancy; *Med. Hypotheses* **46** 362–367

Morris J A 1997 Genetic control of redundant systems; *Med. Hypotheses* **49** 159–164

Morris J A 1999a Effects of somatic cloning; *Lancet* **354** 255

Morris J A 1999b Information and redundancy: key concepts in understanding the genetic control of health and intelligence; *Med. Hypotheses* **53** 118–123

Morris J A 2001 How many deleterious mutations are there in the human genome?; *Med. Hypotheses* (in press)

Oddy W H, Holt P G, Sly P D, Read A W, Landau L I, Stanley F J, Kendal G E and Burton P R 1999 Association between breast feeding and asthma in 6 year old children: findings of a prospective birth cohort study; *Br. Med. J.* **319** 815–819

Redfield R J 1994 Male mutation rates and the cost of sex for females; *Nature* (*London*) **369** 145–147

Shannon C E 1948 The mathematical theory of communication; *Bell Syst. Technol. J.* **27** 379–423