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NUMBER XIV

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AND ANALOGUES
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PREFACE

A symposium of this title could well have been held in Ancient Greece, but it would then have had the assistance of a philosopher: this it was denied through the indisposition of Professor K. R. Popper, who had hoped to contribute. It could have been held in 1900, but again, the particular subject of anatomical homologue and analogue which might have dominated it then, is not now included. The contributors certainly represent a very much wider cross-section of every field of science than has been the case with any previous volume in this series; if it appeared from the programme of the Conference that the titles of contributions bore little relation to one another, the Conference itself certainly concluded with an appreciation of the diversity of approaches which can be made towards a fundamental feature of science, which is particularly critical to the present state of biology. It is consequently hoped that this volume may serve two purposes: to attract the attention of scientists of all disciplines to the problems which are central in biological investigation and communication and to indicate to biologists the forms of approach made to analogous problems in other sciences; to provide a variety of pathways, one of which may lead the student towards these problems of thought, language and biology.

The Conference was held in Queen's Building, University of Bristol from 6 to 12 September, and owed much to many members of that University for their hospitality; Dr R. B. Clark undertook the arduous duties of Local Secretary. Professor T. Weis-Fogh flew from Copenhagen at extremely short notice to deliver Professor Bohr's Paper.

I am much indebted to contributors and colleagues for their suggestions during the planning of the Symposium, and must particularly acknowledge the help of Professor C. F. A. Pantin and Dr K. E. Machin. Finally, it is a pleasure to record the help and co-operation of the Cambridge University Press in the preparation of the volume.

J. W. L. BEAMENT

QUANTUM PHYSICS AND BIOLOGY†

By NIELS BOHR

Institute for Theoretical Physics, University of Copenhagen

I

The significance of physical science for philosophy does not merely lie in the steady increase of our experience of inanimate matter, but above all in the opportunity of testing the foundation and scope of some of our most elementary concepts. Notwithstanding refinements of terminology due to accumulation of experimental evidence and developments of theoretical conceptions, all account of physical experience is, of course, ultimately based on common language, adapted to orientation in our surroundings and tracing of relationships between cause and effect. Indeed, Galileo's programme to base the description of physical phenomena on measurable quantities has afforded a solid foundation for the ordering of an ever larger field of experience.

In Newtonian mechanics, where the state of a system of material bodies is defined by their instantaneous positions and velocities, it proved possible, by the well-known simple principles, to derive, uniquely from the knowledge of the state of the system at a given time and of the forces acting upon the bodies, the state of the system at any other time. A description of this kind, which evidently represents an ideal form of causal relationships, expressed by the notion of *determinism*, was found to have still wider scope. Thus, in the account of electromagnetic phenomena, in which we have to consider a propagation of forces with finite velocities, a deterministic description could be upheld by including in the definition of the state not only the positions and velocities of the charged bodies, but also the direction and intensity of the electric and magnetic forces at every point of space at a given time.

A new epoch in physical science was inaugurated by Planck's discovery of the *elementary quantum of action*, which revealed a feature of *wholeness* inherent in atomic processes going far beyond the ancient idea of the limited divisibility of matter. Indeed, it became clear that the pictorial description of classical physical theories represents an idealization valid only for phenomena in the analysis of which all actions involved are sufficiently large to permit the neglect of the quantum. While this condition is amply fulfilled in phenomena on the ordinary scale, we meet, in experimental evidence concerning atomic particles, with regularities of a novel type, incompatible with deterministic analysis. These quantal laws are determining for the peculiar

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† The author has abbreviated his recent article from *Survey of Philosophy in the Mid-Century*, Firenze, 1958, to form the first portion of his paper, while the remainder he specially prepared for this Symposium.

stability and reactions of atomic systems, and thus ultimately responsible for the properties of matter on which our means of observation depend.

In spite of the power of quantum mechanics as a means of ordering an immense amount of evidence regarding atomic phenomena, its departure from accustomed demands of causal explanation has naturally given rise to the question whether we are here concerned with an exhaustive description of experience. The answer to this question evidently calls for a closer examination of the conditions for the unambiguous use of the concepts of classical physics in the analysis of atomic phenomena. The decisive point is to recognize that the description of the experimental arrangement and the recording of observations must be given in plain language, suitably refined by usual physical terminology. This is a simple logical demand, since by the word experiment we can only mean a procedure about which we are able to communicate to others what we have done and what we have learnt.

In actual experimental arrangements, the fulfilment of such requirements is secured by the use as measuring instruments of rigid bodies sufficiently heavy to allow a completely classical account of their relative positions and velocities. In this connexion, it is also essential to remember that all unambiguous information concerning atomic objects is derived from the permanent marks—such as a spot on a photographic plate, caused by the impact of an electron—left on the bodies which define the experimental conditions. Far from involving any special intricacy, the irre.ersible amplification effects on which the recording of the presence of atomic objects rests rather remind us of the essential irreversibility inherent in the very concept of observation. The description of atomic phenomena has in these respects a perfectly objective character, in the sense that no explicit reference is made to any individual observer and that therefore, with proper regard to relativistic exigencies, no ambiguity is involved in the communication of information.

As regards all such points, the observation problem of quantum physics in no way differs from the classical physical approach. The essentially new feature in the analysis of quantum phenomena is, however, the introduction of a *fundamental distinction between the measuring apparatus and the objects under investigation*. This is a direct consequence of the necessity of accounting for the functions of the measuring instruments in purely classical terms, excluding in principle any regard to the quantum of action. On their side, the quantal features of the phenomenon are revealed in the information about the atomic objects derived from the observations. While, within the scope of classical physics, the interaction between object and apparatus can be neglected or, if necessary, compensated for, this interaction, in quantum physics, thus forms an inseparable part of the phenomenon. Accordingly, the unambiguous account of proper quantum phenomena must, in principle, include a description of all relevant features of the experimental arrangement.

The very fact that repetition of the same experiment, defined on the lines described, in general yields different recordings pertaining to the object,

immediately implies that a comprehensive account of experience in this field must be expressed by statistical laws. It need hardly be stressed that we are not here concerned with an analogy to the familiar recourse to statistics in the description of physical systems of too complicated a structure to make practicable the complete definition of their state necessary for a deterministic account. In the case of quantum phenomena, the unlimited divisibility of events implied in a deterministic account is, in principle, excluded by the requirement to specify the experimental conditions. Indeed, the feature of wholeness typical of proper quantum phenomena finds its logical expression in the circumstance that any attempt at a well-defined subdivision would demand a change in the experimental arrangement incompatible with the definition of the phenomenon under investigation.

Within the scope of classical physics, all characteristic properties of a given object can in principle be ascertained by a single experimental arrangement, although in practice various arrangements are often convenient for the study of different aspects of the phenomena. In fact, data obtained in such a way simply supplement each other and can be combined into a consistent picture of the behaviour of the object under investigation. In quantum physics, however, evidence about atomic objects obtained by different experimental arrangements exhibits a novel kind of complementary relationship. Indeed, it must be recognized that such evidence, which appears contradictory when combination into a single picture is attempted, exhausts all conceivable knowledge about the object. Far from restricting our efforts to put questions to nature in the form of experiments, the notion of *complementarity* simply characterizes the answers we can receive by such inquiry in the case when the interaction between the measuring instruments and the objects forms an integral part of the phenomena.

The question has been raised whether recourse to multivalued logics is needed for a more appropriate representation of the situation. From the preceding argumentation it will appear, however, that all departures from common language and ordinary logic are entirely avoided by reserving the word 'phenomenon' solely for reference to unambiguously communicable information, in the account of which the word 'measurement' is used in its plain meaning of standardized comparison. Such caution in the choice of terminology is especially important in the exploration of a new field of experience, where information cannot be comprehended in the familiar frame which in classical physics found such unrestricted applicability.

In general philosophical perspective, it is significant that, as regards analysis and synthesis in other fields of knowledge, we are confronted with situations reminding of that in quantum physics. Thus, the integrity of living organisms and the characteristics of conscious individuals and human cultures present features of wholeness, the account of which implies a typical complementary mode of description (Bohr, 1958). Due to the diversified use of the rich vocabulary available for communication of experience in those wider fields,

and above all to the varying interpretations, in philosophical literature, of the concept of causality, the aim of such comparisons has sometimes been misunderstood. However, the gradual development of an appropriate terminology for the description of the simpler situation in physical science indicates that we are not dealing with more or less vague analogies, but with clear examples of logical relations which in different contexts are met with in wider fields.

II

The discussion of the position of living organisms in a general description of physical phenomena has, in the development of science, passed through a number of stages. In Antiquity, the obvious difficulties inherent in a comparison between organisms and primitive machinery deeply influenced the attitude towards mechanical problems and even led to the attribution of vital characteristics to all matter. With the abandonment of these views, at the time of the Renaissance, through the clarification of the principles of classical mechanics, the problem entered into another stage, stimulated by the great anatomical and physiological discoveries at that period.

Recent advances in technology, and especially the development of automatic control of industrial plants and calculation devices, have given rise to a renewed discussion of the extent to which it is possible to construct mechanical and electrical models with properties resembling the behaviour of living organisms. Indeed, it may be feasible to design models reacting in any prescribed manner, including their own reproduction, provided that they have access to the necessary materials and energy sources. Still, quite apart from the suggestive value of such comparisons, we must realize that, in the study of models of given structure and functions, we are very far from the situation in which we find ourselves in the investigation of living organisms, where our task is gradually to unravel their constitution and capacities.

In any model on the ordinary scale, we can essentially disregard the atomic constitution of matter and confine ourselves to the account of the mechanical and electrical properties of the materials used for the construction of the machine and to the application of the simple laws governing the interaction between its parts. From biological research, however, it is evident that fundamental characteristics of living organisms, and in particular genetic reproduction, depend primarily on processes on the atomic scale, where we are faced with essential limitations of the applicability of the concepts of classical physics.

As is well known, quantum physics offers a frame sufficiently wide for the account of properties of atoms entirely beyond the grasp of classical approach. A main result of this development is the recognition of a peculiar stability of atomic and molecular structures, which implies a degree of order incompatible with the unlimited use of mechanical pictures. The deterministic

account of classical physics which implies that any disturbance of a system composed of an immense number of parts invariably leads to chaotic disorder, is in quantum physics replaced by a description according to which the result of any interaction between atomic systems is the outcome of a competition between various individual processes by which the states of the new systems, like those of the original systems, in a simple way are defined by the atomic particles they contain. With suitable adjustments, this description directly corresponds to the chemical kinetics which has found extensive application in molecular biology.

Quite novel prospects of a gradual elucidation of biological regularities on the basis of well-established principles of atomic physics have been opened in later years by the discoveries of the remarkably stable specific structures carrying genetic information, and the increasing insight into the processes by which this information is transferred. Indeed, the view suggests itself that, in metabolism, the formation and regeneration of the persistent constituents of the organism are to be regarded as processes of essentially irreversible character which at any step secure the greatest possible stability compatible with the prevailing conditions as regards material and energy exchange.

Although, thus, we have no reason to expect any inherent limitation of the application of elementary physical and chemical concepts to the analysis of biological phenomena, the peculiar properties of living organisms, which have resulted from the whole history of organic evolution, reveal potentialities of immensely complicated material systems, which have no parallel in the comparatively simple problems with which we are concerned in ordinary physics and chemistry. It is on this background that notions referring to the behaviour of organisms as entities, and apparently contrasting with the account of the properties of inanimate matter, have found fruitful application in biology.

Even though we are here concerned with typical complementary relationships as regards the use of appropriate terminology, it must be stressed that the argument differs in essential aspects from that concerning exhaustive objective description in quantum physics. Indeed, the distinction demanded by this description between the measuring apparatus and the object under investigation, which implies mutual exclusion of the strict application of space-time co-ordination and energy-momentum conservation laws in the account of individual atomic processes, is already, as indicated above, taken into account in the use of chemical kinetics and thermodynamics. The complementary approach in biology is rather required by the practically inexhaustible potentialities of living organisms entailed by the immense complexity of their structures and functions.

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MODELS IN GENETICS

By A. W. F. EDWARDS†

Department of Genetics, University of Cambridge

Genetics is the study of the biological relations between parent and offspring. Some of the observed similarities are due to the environmental influence of parent on offspring, or of a similar environment on both, whilst others are due to the transmission of matter, influential in the moulding of the offspring, by the parental zygotes. Classical genetic theory tells us that genes, spaced along chromosomes in the nucleus of a cell, and transmitted from parent to offspring, control the development of the individual.

Opportunities for physical models in genetics are many: from those showing the behaviour of chromosomes at meiosis, to those portraying the most recent advances, such as the model of the bacteriophage, or of the double-spiral structure of DNA. But we will concern ourselves here with a model of much wider application: the mathematical model 'probability'.

The concept of probability is very widely used in genetics. It is used in mathematical models of populations and of evolutionary changes, in techniques—such as in the sample-recapture method of estimating population size, in statistical tests, and in the mathematical model of the segregation of characters. It is this particular model that we will analyse.

Gregor Mendel was the first person to examine the segregation of characters critically, and his extensive experiments led him to formulate his famous Law of Segregation of genes. Not only did he observe that the segregation ratios, as we now call them, were integral ratios such as one-to-one, or three-to-one, but he also put forward the concept of a gene to explain how such segregations arose. Upon the foundation that he laid geneticists have built a statistical model which is compatible with the observed segregation ratios.

This model is wholly based on the concept of probability. We postulate that a crossover in a certain part of a chromosome will occur with probability p_1, that a certain centromere will go to a certain nucleus at division with probability p_2, and so on. Then we compound our postulated probabilities according to the mathematical laws of probability, and obtain expectations for the segregation ratios. Finally, knowing the observed segregation ratios, we derive estimates for $p_1, p_2, \ldots$ by an approved statistical technique, and we are left with a probability model describing a biological process.

We must now digress into a consideration of what we mean by a model: How does it differ from a description, or a law? Must it have a logical structure? May we logically draw any conclusions from one?

First, a model need not be physical: it can be mathematical, or it can exist merely in the mind of the scientist. For example, when Laplace writes 'in

order to convince ourselves, let us take two urns, A and B, the first containing four white and two black balls, and the second containing only two white balls and one black one' he is not saying that he has actually done this, nor is he suggesting that we should. He just wants us to *imagine* that we do this, thereby helping our understanding of the problem. A model, then, must be positive: it must help us to reason and to understand. A description is negative; by itself it does not help us to understand, and it is therefore not a model.

On the other hand a law is a model, either mathematical or conceptual, although a model is, of course, not necessarily a law. In general models, including laws, are only approximate. We can refine them as much as we like, but they are still not exactly verifiable, owing to the limits of experimental accuracy. They are accurately obeyed only in the model world that exists at the back of a scientist's mind. In the past many scientists, especially physicists, have believed implicitly in their models, thinking that any deviation of their observations from them can be dismissed in the word 'error'. But this error is absolutely fundamental. Not only are we incapable of measuring precisely, but we cannot be sure that the very act of measuring does not change that which is being measured. This fact is well borne out in the microscopic world, where Heisenberg's Principle of Uncertainty gives a lower limit to the possible error.

There may be, however, just one kind of model that can be exact within its own limitations. The model based on probability may be exact, because it makes allowance for the error, and admits our partial ignorance, and this is why it is such a vitally important model in modern science.

Next, we ask whether a model must have a logical structure. With a physical model there is clearly no difficulty here. But in a conceptual model are we permitted to conceive something which cannot possibly exist? This question is very fundamental, and there is much disagreement about it. If we ask whether the sex ratio differs significantly between Bristol and Bath, are we at liberty to imagine an infinity of Bristols and Baths in order to make our test of significance? Or can we talk sensibly in terms of limiting probability when that is only defined at the end of an infinite series of trials? This question must remain unanswered, here, for it strikes at the very root of a deep controversy.

Last, we asked whether we may draw any conclusions from a model. Clearly, in general, we may not; even with a mathematical law, every logical deduction is open to experimental verification, and if it is unverified, the law is discarded as being inapplicable. A model may point the way, but it must not lead us. The exception is the probabilistic model. Here we may make inferences, in terms of probability statements, about the real world.

In order to satisfy ourselves as to the logical structure of the particular genetical model in which we are interested, we see that it is necessary to examine the concept of probability itself. Unfortunately the theory of prob-

ability and scientific inference is in a state of flux. There is a great deal of controversy about the meaning and definition of probability, and further controversy about the drawing of probabilistic inferences. In order to by-pass this controversy we will define the model under consideration in terms of the Fisherian approach, so that it subscribes to R. A. Fisher's views (1956) on probability, randomness, and scientific inference. To do so is not to presume the logical soundness of the Fisherian approach, but rather to admit that that approach, if not sound, is a good approximation to reality.

The meaning of probability in the Fisherian scheme may now be explained. First there is prior probability; secondly there is posterior probability, and thirdly there is mathematical probability. Consider an experiment with dice and suppose that A is a physicist, and B is not. By making careful measurements of a die, A may conclude that it is biased, and that his estimate of the proportion of trials that will result in a 'six' is not one-sixth, but one-fifth. That is A's prior probability. Not knowing that the die is biased, B's estimate is one-sixth. Both estimates are meaningful, but A's is based on a greater degree of knowledge than B's. The fact that prior probabilities may differ from person to person when considering the same thing invites one to call them subjective, which, indeed, Poincaré does.

Posterior probability is, however, rather more objective, and is the *result* of a series of trials convoluted with the prior probability of success in that series. It is thus an improvement on the prior probability as it includes our experience of what has actually happened. It is only entirely objective when no prior probability is available, or when the prior probability is estimated solely from the results of previous trials. For the posterior probability of one set of trials is the prior probability of the next set. Mathematical probability is the true probability of success in a trial (a very questionable concept) and as such prior and posterior probability are estimates of it: the more trials we do, the better the estimates. The statistician thus pictures the learning process as shown in Fig. 1.
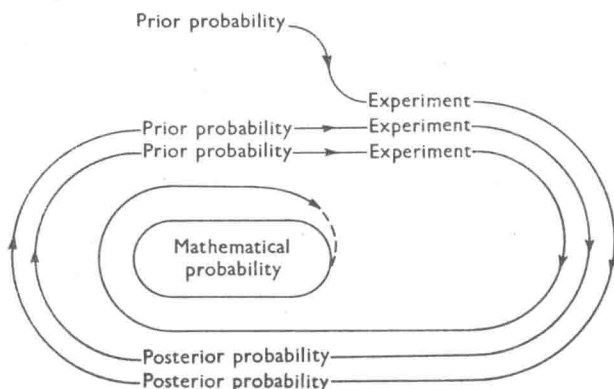

Fig. 1. Statistical interpretation of the learning process.

Bearing these meanings in mind, we can now demonstrate how useful the probabilistic model of segregation ratios has been. When Mendel first proposed the model it gave a satisfactory account of the two-factor segregations with which he was working. However, soon after the re-discovery of Mendel's papers it was noticed that sometimes two different characters tended to segregate together, and in 1911 Morgan, in America, realized that the two loci concerned were probably linked together by being on the same chromosome. The original discovery was made because it was noticed that the probability models for the two loci were not independent. So a new parameter, the recombination fraction, was introduced, and the two models combined; thus was the statistical study of linkage between loci born.

When more than two linked loci were studied simultaneously (Müller, 1916) it soon became apparent that crossing-over between two of the loci inhibited, or interfered with, crossing-over between another pair, and that one could not treat each pair of loci independently. So a further synthesis was made, and a more general model created which dealt with each chromosome as a unit. Thus arose the genetical theory of interference, which Owen (1950) has done much to develop. This model was satisfactory until Michie & Wallace (1953) noticed some strange segregations in experimental populations of house mice, and to explain these the concept of affinity was introduced; it seems that chromosomes themselves do not segregate independently after all.

All these advances were the result of testing observed segregations against the current probability model, and it is an indication of the power of the model that each advance was made before the corresponding cytological facts were known.

So far we have considered inferences that have been made with the help of observations on the means of distributions of segregations, but we can go on to consider the variances, first establishing some of the statistical properties of the distributions. For simplicity we will deal with a binomial segregation, that is, a series of trials each of which can only result in one of two possibilities. For example, in a mating $AA \times Aa$ the only possible progeny are AA and Aa. The general problem with more than two possibilities requires knowledge of the multinomial distribution. Let the mathematical probability of a birth being of genotype AA be p, and of genotype Aa be q, so that $p+q = 1$. In a family of N births, the probability of getting exactly r AA and $(N-r)$ Aa in a certain order is $p^r q^{N-r}$. This is found by multiplying up the probabilities at each birth. But there are $\dfrac{N!}{r!(N-r)!} = \dbinom{N}{r}$ possible orders, all equally likely, so that the total probability of getting exactly r AA in a family of N is $\dbinom{N}{r} p^r q^{N-r}$. This is the general term of the binomial distribution. In Table 1 we give the distribution for $p = \frac{1}{4}$, $N = 8$, using a hundred families. We expect observations of segregations in one hundred families of eight, in which $p = \frac{1}{4}$, to fit this distribution more-or-less closely, and there are statis-

tical tests available to tell us whether the fit is unreasonably bad, or, indeed, unreasonably good. It is a matter of interest that the fit of Mendel's distribution is unreasonably good, and Fisher (1936) has suggested that the Abbot's gardeners were rather too keen to please him.

Table 1.

$r = 0$	Frequency $= 10$
1	27
2	31
3	21
4	9
5	2
6	0
7	0
8	0
	100

Since the mathematical probability p is unknown, we use the posterior probability in calculating the terms of the distribution, and, if prior information does not exist, this is equivalent to equating the observed mean of the distribution to Np, the theoretical mean. Using this estimate of p we may calculate the expected variance Npq and if p has not varied significantly between families, and between births in each family, this variance will not differ significantly from the variance calculated from observations. Now when a geneticist carries out an experiment and records the segregations, he does not usually work out the expected variance of the distribution and see if it agrees with his observations. He does often employ tests for heterogeneity between families, but these are rather less informative. This is, possibly, a bad omission, for if he were to do so he might learn about the variability of the probability in which he is interested, in the following way:

Suppose that N trials constitute an experiment, and a series of experiments constitutes a test. In the terminology we have been using, a trial corresponds to a birth, an experiment to a family, and a test to a set of data comprising several families. If the mathematical probability of success varies between experiments, as it would if the subject of each experiment were a different penny with a different bias, and if the overall probability of success is p, then it is not difficult to see that the variance of the resulting distribution will be greater than Npq. It is as though one were adding many binomial distributions with different values of p together; in the limit, if p were 0 in half the experiments, and 1 in the rest, the resulting distribution would consist of just the two end classes, no successes and N successes. At the end of the last century the German economist W. Lexis (see Weatherburn, 1952) investigated this type of distribution, and found that its variance exceeded Npq by an amount $N(N—1)$ times the variance of p between experiments. Thus, if the observed variance is greater than that expected on the simple binomial hypothesis one can estimate the variance of p between experiments that would

explain the excess. The only genetical segregation for which this has been done is the human sex ratio (Edwards, 1958).

On the other hand, suppose that p varies within an experiment, but that it varies in the same way for each experiment. This is like having N pennies, each of different bias, and using each penny once in each experiment. S. D. Poisson (see Weatherburn, 1952) worked out what happens to the variance in this case, and found that it was *less* than Npq by an amount N times the variance of p within experiments. It is surprising, at first sight, that the variance should be reduced, but again a limiting argument is convincing: if p takes on the value 0 in half the trials, and 1 in the rest (supposing N, the number of trials in an experiment, to be even), then all the experiments will result in exactly $N/2$ successes, and the distribution will have no variance at all. Thus a series of segregations with the observed variance less than the expected is also possible. It was observed, for example, by A. S. Parkes (1923) in his data on the sex ratio in pigs, where one litter corresponded to an experiment, and it looks as though there was variability in the probability of a birth being male within litters. This variability can be estimated from the observed variance.

If one type of variation of the probability can cause an increased variance, and another a reduced variance, it is clear that we cannot separate the two effects by examining variances alone, and we may only estimate the magnitude of one cause if we are sure of the magnitude of the other. Nevertheless, in practical situations useful estimates may be made.

Thus, by calculating the variances of our distributions, additional information may be gained, although it would be incorrect to infer from the lack of an abnormal variance that the trials were all of the same probability, for the two effects may be cancelling one another out.

This has some genetic interest from another point of view. Suppose that A gives B a bag containing a large number of pennies which are all biased by different amounts, and tells him to pick out a penny at random, to toss it, and to record the result. B is to construct a binomial series of trials in this way. A has not told B that there is anything odd about the pennies, and wants him to make what inferences he can about them. On doing this B finds that the resulting distribution fits the simple binomial admirably, and infers that the probability of 'heads' was constant from toss to toss, and that the pennies in the bag were all unbiased ones. The fallacy of this argument lies in the fact that the pennies were chosen at random, so that even though they had different degrees of bias, the chance of 'heads' was indeed constant from toss to toss. The changes in the variance which have been described above cancel out precisely.

This fallacy has a parallel in genetics. The point it illustrates is that the process of randomization destroys information that would otherwise be available. In the case of the pennies, the fact that A told B to draw each one at random from the bag immediately destroyed any hope B may have had of