COMETS, CONTAGION AND CONTINGENCY

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Summary

Two astronomers, F. Hoyle and C. Wickramasinghe, have collected data on various epidemics in schools in an attempt to show that person to person transmission alone is unable to explain the pattern of disease and that outside contamination from a cometary source must therefore be considered. It is explained here, with the help of an artificial model, why their analysis is inadequate. It is shown that the problem of deciding between the 'conventional' hypothesis and the 'cometary' hypothesis is one of deciding between competing clustering processes, that this is no easy task, and that data in the form in which Hoyle and Wickramasinghe have collected them are unsuitable for this purpose.

'The question arises here whether or not the comet Venus infested the earth with vermin which it may have carried in its trailing atmosphere in the form of larvae...'

Immanuel Velikovsky[1]

> *'...it does not seem to be entirely out of the question that the eggs and sperms of insects might once have been arrivals from space...'*
>
> *Fred Hoyle*[2]

Introduction

In the preface to the paperback edition of his controversial best selling work of cosmology, *Worlds in Collision*[1] , Immanuel Velikovsky, reviewing the reaction to the first appearance of his theories in 1950, had cause to refer to a British astronomer's discussion of the evolution of scientific knowledge in the following terms:

In 1950 it was generally assumed that the fundamentals of science were known and that only decimals were left to fill in. In the same year a cosmologist, certainly not of a conservative bent of mind, Fred Hoyle, wrote in the conclusion of his book, The Nature of the Universe: '*Is it likely that any astonishing new developments are lying in wait for us? Is it possible that the cosmology of 500 years hence will extend as far beyond our present beliefs as our cosmology goes beyond that of Newton?' And he continued: 'I doubt whether this will be so. I am prepared to believe that there will be many advances in detailed understanding of matters that still baffle us ...But by and large I think that our present picture will turn out to bear an approximate resemblance to the cosmologies of the future'.*

By a curious irony, which Immanuel Velikovsky could hardly have foreseen, within a few years. Fred Hoyle himself, in association with another

astronomer and mathematician, Chandra Wickramasinghe, was to publish a theory regarding the origins of life which was to attract reactions similar in terms of hostility and incredulity to those which had greeted the appearance of Worlds in Collision a quarter of a century before, and which, were it to be commonly accepted as true, would require a similar cataclysmic revolution of accepted scientific dogma[2,3,4,5,6,.]

Although Velikovsky and Hoyle and Wickramasinghe have mounted very different attacks on accepted cosmology, in particular the inspiration for the two theories (historical in the case of Velikovsky and astronomical for Hoyle and Wickramasinghe) is quite different, the theories have curious similarities. Both of these extraordinary cosmologies attack accepted theories of evolution and paleontology, both accept the possibility of extra-terrestrial life (although this has differing degrees of importance for the two theories), both have led the authors to make successful predictions about other members of the solar system (Venus, Jupiter and the moon in the case of Velikovsky, Halley's comet in the case of Hoyle and Wickramasinghe), and both sets of authors have found their predictions explained away after they have been fulfilled[7,8.] A final irony, which would not, however, surprise Immanuel Velikovsky, is that there is no reference to his work in *Diseases from Space.*

This article is concerned with the latter of these two theories or more precisely with one particular aspect of it: Hoyle and Wickramasinghe's contention that certain epidemics can only be explained in terms of contamination from bacteria or viruses falling through the earth's atmosphere and having their origin in comets. Two important points need to be made before starting the examination of this aspect. First that Hoyle and Wickramasinghe's theories deserve to be taken seriously - if true they have enormous implications for every scientific discipline including medicine and statistics, if false they nevertheless serve to expose the extent to which many of the 'facts' we take for granted are no more than a habit of thinking. Secondly that although the course and pattern of epidemics is an important element in the cometary hypothesis it is only one of many, and it is possible that developments in other fields may render statistical analysis an irrelevant means of examining the

cometary theory. Nevertheless if seeking to join this cosmological debate the medical statistician can do no better than pose himself the question that Immanuel Velikovsky advises all would be cosmologists to consider: 'Which part of the work is committed to us?'. It is the purpose of this article to explain how at least in general qualitative terms a number of the epidemics which Hoyle and Wickramasinghe have reported can be explained in terms of conventional theories of person to person transmission. If the reader is disappointed by the lack of a more rigorous and mathematical element in what is to follow it will perhaps serve as excuse to note that a theory may be adequately defended in the terms in which it is attacked but also to remark that another purpose of this review is to encourage other statisticians, more suitably qualified for the task than the author, that this is a general area worth investigating and debate worth joining.

If any further justification for the topic is required it is perhaps worth remarking that a recent editorial in the Lancet on the subject of the common cold, whilst finding no space to discuss the comentary hypothesis, nevertheless began as follows: 'Everyone knows what it is like to catch a cold, yet we know surprisingly little about how it happens. Years ago we thought we knew.'[9] There are many puzzling features of epidemics which do not at first sight accord well theories of person to person transmission and the medical statistician might do worse than to follow D.V. Lindley's advice regarding that prejudice which Bayesians refer to as prior belief: 'so leave a little probability for the moon being made of green cheese; it can be as small as 1 in a million, but have it there since otherwise an army of astronauts returning with samples of the said cheese will leave you unmoved.'[10] All that it is necessary to add to this is a warning to the reader not to dismiss the comentary theory out of hand without first reading what Hoyle and Wickramasinghe have to say about it; like the theories of Immanuel Velikovsky it has subtleties which may embarrass rash attempts to dismiss it.

Mathematical Epidemiology

Mathematical epidemiology also conceals traps for the unwary and if Hoyle and Wickramasinghe have had cause to complain that the range and subtlety of their theories have been underestimated and their nature misrepresented and misunderstood it may reasonably be said that they have committed the same sin with regard to mathematical epidemiology. In this context it is worth reviewing a number of important features of epidemic models.

The first is that the distributions of numbers infected to which epidemiological models give rise have large variances. One of the simplest of contagious models leads to the negative binomial, a distribution which, in any empirical investigation in which extra-Poisson variation is discovered is often the first to be considered. Even the negative binomial, however, frequently understates the case as regards variability, and as a number of authors have noted, given suitable parameter combinations, U shaped distributions can be produced[11,12.]

The second feature is that very different models of disease may give rise to identical distributions. An interesting paper of Neyman's discusses the way in which a process corresponding to true contagion, can give rise to multivariate distributions with identical margins[13.] He also gives a varied list of phenomena to which a further clustering model may be applied: the distribution of larvae in the field, the clustering of galaxies, population theory, and, two applications which are extremely interesting in the present context: the theory of epidemics and the investigation of bombing by formations of planes.

The third feature is the historical one that elaborate theories of disease mechanism have, on occasion, been rendered superfluous by suitable developments in mathematical modelling. One such is Brownlee's theory of exponential decay in infectivity. A fascinating account of the circumstances which lead Brownlee to incorporate this feature into his mathematical models is given in an exvellent review by Paul Fine[14] (which in no way concerns itself with the theories of Hoyle and Wickramasinghe). Brownlee's theory is now

regarded as a result of semantic and mathematical flaws but three points from Fine's review may be of interest to defenders of the Hoyle- Wickramasinghe hypothesis. The first is Fine's description of Brownlee as having the misfortune, 'to have worked at a time when his subject was making the radical shift from miasma to germ'. This is a shift which Hoyle and wickramasinghe are seeking (in some sense) to reverse and its acceptance as fact should not of course be considered in any analysis of their work. The second is Fine's interesting reference to William Farr's successful predictions of the course of epidemics *despite* believing in the miasma theory. The third is his discussion of a particular problem for Brownlee's theory: the fact that epidemics recur requires organisms to regain their infectivity if they also lose it during the course of an epidemic. This is not a problem for Frost's epidemic model which was the first to avoid Brownlee's mass-action fallacy and is now part of mainstream mathematical epidemiology but then it ought to be noted that it is not a problem for the Hoyle-Wickramasinghe hypothesis either if the recurrence of epidemics results from repeated encounters with a source of infectivity maintained in historic condition by the environment of outer space.

The fourth point, related perhaps to the previous three, is that naive reason is not a very safe guide when discussing the effects of changes in conditions or assumptions in the field of mathematical modelling and counter-intuitive results may obtain. For example, recent work on the modelling of the spread of AIDS has led to the discovery that under certain circumstances individuals of moderate promiscuity may be at equal risk to those of high promiscuity[15.] Similarly under certain circumstances an increase in rubella vaccination may lead to a rise in the numbers of babies born with rubella related syndrome[16.] Returning to AIDS again for a third example it is not necessarily the case that the higher the proportion of persons with HIV infection who go on to develop full blown AIDS the greater will be the eventual number of deaths from this condition. Barlett's remark, 'that complex and certainly not obvious consequences flow from even the simplest model,' is an appropriate warning[17.]

Finally a fifth point of importance is that unlike other problems in medical statistics, in mathematical epidemiology, probability is affected by data order. Thus in chain binomial theories the sequence in which cases occur carries information which is lost by a summary in terms of totals affected and this is a striking difference from the standard binomial.

A consequence of all these elements is that definitive identification of underlying process using totals infected classified by location is an extremely difficult task which requires very careful thought and may in many cases prove impossible. An excellent review of attempts to investigate the supposed phenomenon of leukaemia clustering by Smith[18] makes clear just how difficult this task may be. In such a case, however, the null hypothesis (that of no infection) at least makes possible the calculation of the size of various tests even if the power of such procedures is often unknown. In making their challenge to conventional epidemiology, however, Hoyle and Wickramasinghe pose a much more difficult problem and one whose nature they have misunderstood: one of deciding between competing clustering processes. If Neyman could find the same distribution applicable to infectious disease and bombing patterns, the problem of deciding between person to person transmission and infection as a result of bacterial rain is no easy matter.

In fact, as Bates' solution to the false and true contagion problem shows, progress can sometimes be made in deciding between epidemic processes given adequate models and suitable data[19.] As will be shown below, however, Hoyle and Wickramasinghe have neither.

An Illustrative Model

Before proceeding to a discussion of Hoyle and Wickramasinghe's data and methods, however, a simple model will be reviewed in order to be able to illustrate a number of peculiar features of contingency tables when these represent data from epidemics[20.] Lest there is any danger of the purpose of this model being mistaken, it should be clearly understood that it is not being

proposed as a means of practical investigation but simply because it is adequate for illustrating the effect of clustering on contigency analysis.

Imagine a population of n individuals arranged in a circle. Each individual can infect either or both his neighbours. Imagine that a disease appears in this community as a result of a single introduction and that it is characterised by a fixed serial interval and a short period of infectivity. If X is the final number of cases infected and 🖹 is the probability that a currently infectious individual will infect a given, adjacent, uninfected individual, then, given that an epidemic has started we have,

$$P(X=x) = x\theta^{x-1}(1-\theta)^2 \qquad x \leq n-1$$

$$= (n-1)\,\theta^{n-1}(1-\theta) + \theta^{n-1} \qquad x = n$$

Next suppose that we have an even number of individuals in the population and that $n/2$ may be classified as type A and $n/2$ as type B. Suppose that the pattern of social contacts in such that the individuals are arranged such that the As are together and the Bs are together and there are two points of contact.

Let the random variable Y represent the final number of infected cases of type A. A simple geometric argument then shows that the conditional distribution of Y given X is given by

$$P(Y=y \mid X=x) = 2/n \qquad , 0 < y < x$$
$$= \{n-2(x-1)\}/(2n) \qquad , y=0 \text{ or } y=x$$
$$= 0 \qquad , \text{elsewhere,}$$
$$x \leq n/2$$

$$= 2/n \qquad , x-n/2 < y > n/2$$
$$= \{n-2(n-x-1)\}/(2n) \qquad , y=n/2 \text{ or } y=x-n/2$$
$$= 0 \qquad , \text{elsewhere,}$$

$x \geq n/2$.

For ease of discussion this will be referred to as the *ring distribution*.

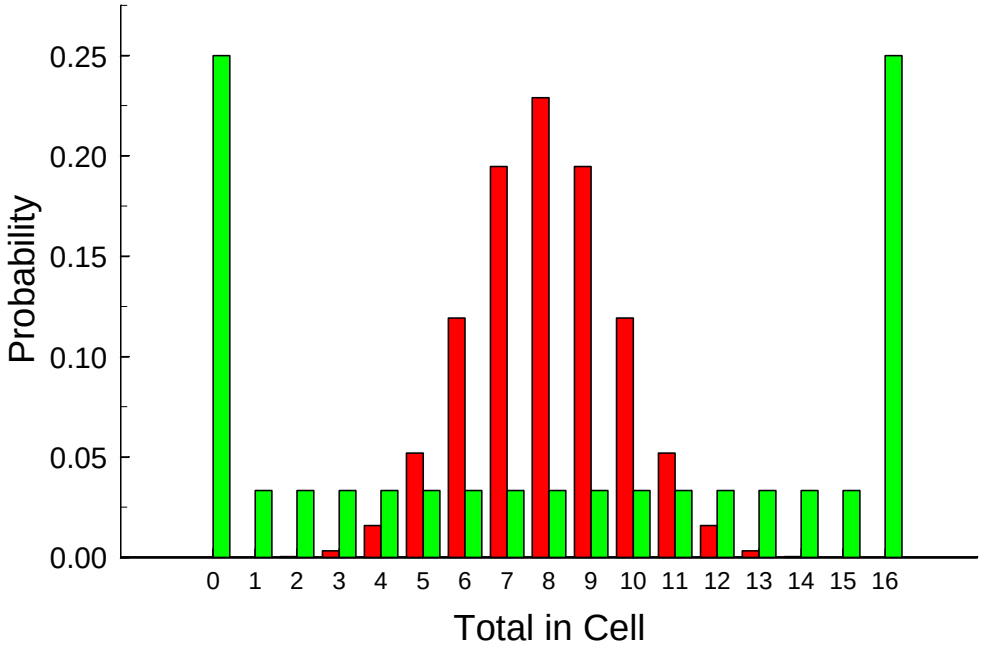
Table 1
Contingency Table Associated
With Spatial Epidemic Model

	A	B	
Infected	y	x-y	x
Not Infected	n/2-y	n/2-x+y	(n-x)
	n/2	n/2	n

Also note, however, that corresponding to this model is the contingency table given by table 1. Now it is interesting to consider what the consequence is of applying standard techniques of analysis for contingency tables to such a model. Suppose we evaluate the probability of every possible table having marginal totals $n/2$, $n/2$, x and n-x. Such tables may be indexed by the number of infected *A*s, Y, and therefore the probability distribution of the tables is that of Y given X above. The usual test for such a table, however, is Fisher's exact test which uses the hypergeometric distribution. Figure 1 compares the probability plot for the hypergeometric distribution (red) and the ring distribution (green) when n=60 and x=16. The U shaped character of the ring distribution is in stark contrast to the unimodal hypergeometric.

Figure 1

probability plot for values of cell in four-fold table with margins of 16 and 30 and total of 60



Clearly the usual tests of association cannot be applied to such a table. The underlying assumptions of within cell independence that such methods (e.g. chi-square analysis) require are not valid. Of course it may be argued that what has invalidated this test is the underlying spatial clustering of the As and Bs. If these characteristics themselves had been independently distributed across the population, the chi-square test of association would be valid whatever the underlying epidemic process. The simple model serves to make a point, however, namely that for numbers infected, standard tests are not *in general* valid for the purpose of investigating association with spatial factors. This point will be considered in more detail below, but, for a recent example of an epidemic which was incorrectly analysed because the investigators failed to appreciate this feature see Senn's discussion of Dupuis et al [21,22.]

There is another important point which this model serves to raise, however, namely, that even the appropriately calculated distribution of usual test statistic (e.g. chi-square) under the null hypothesis is not sufficient to provide an adequate test. For example in this particular case it is not at all clear, without further investigation, what is an appropriate partition of the sample space for deciding between good and bad model fit. In this particular instance, unlike for standard contingency problems, high values of the chi-square might be taken as an indication of good model fit.

Of course in general it is not possible to produce most powerful tests without considering alternative hypotheses. The exact nature of the appropriate alternative hypothesis, for example, has been one of the problems in the search for possible infectious clusters of leukaemia, already referred to[12.] For this particular problem, however, the underlying null hypothesis at least (i.e that of no clustering) is relatively simple and leads to unimodal (i.e n shaped) distributions for which standard measures of discrepancy (such as, e.g, squared distance measures) may at least be presumed to be related (if imperfectly) to that statistic which would be used for the most powerful test were a characterisation of the alternative hypothesis available. If the null hypothesis itself requires clustering, however, no adequate test can be

devised unless the alternative clustering process associated with the alternative hypothesis can be modelled.

One final point can be made profitably using this model. Although for all the reasons given above judgements as to whether or not the model is tenable may be difficult to make using totals infected, the same may not be the case if certain ancillary information becomes available. For example, the observation that three persons had become infected in a given period, or that there had been a period (longer than the serial interval) with no new infections in the middle of the epidemic, or that there was more than one epidemic chain, would each be sufficient to invalidate the model in the strict form in which it is defined above.

Statistics from Space

Hoyle and Wickramsinghe have presented many different arguments in favour of their theory over the last ten years. We are only concerned with the statistical ones here, and the most relevant of all their works in this context is Diseases from Space[5.] The table below is taken from that book and gives data from an epidemic at Howell's school in 1978 and shows the distribution of infected cases amongst two groups adjacent houses.

Table 2

Pupils at Howell's School
Classified by Location and Condition

House Grouping

	Hazelwood & Taylor	Oaklands & Bryn Taff	Total
Infected	26	10	36
Not Infected	25	39	64
TOTAL	51	49	100

Hoyle and Wickramsinghe present their analysis of the null hypothesis of person to person transmission in the following terms ' So what was the chance, if one were to make a random allotment of 36 apples into two essentially equal boxes, of finding that 26 apples had gone into one of the boxes and only 10 into the other box? ....And if one were to include all the still more unequal possibilities, such as 27 apples going into one box and only 9 into the other, 28 into one box and 8 into the other, and so on, the chance of any one of these unusual distributions would be 1 in 100'.

This argument, of course ignores some of the conditioning on the table, but (if such a probability process were appropriate) could be excused on two grounds. First that Diseases from Space is addressed as much to the general public as to fellow scientists, Hoyle and Wickramasinghe feeling perhaps that the former body may be capable of flexibility of thinking the latter are unlikely to develop. Secondly, in many of the other epidemics presented in Diseases from space the calculated significance level is so low as to render such

refinements of calculation as correctly conditioning on margins an irrelevancy. (See, e.g, the data they present on an epidemic at Eton College).

What is extraordinary (and revealing) about the argument is the analogy made and the blatantly inappropriate assumption of independence it implies. If the appropriate model is of some blindfolded cosmic green grocer distributing cases of disease amongst the houses it is unclear as to why this should have any more relevance to an infectious process than to the cometary model, indeed it could be regarded as being more relevant to the latter. A more telling analogy, surely, would be to consider a crate full of apples some of which have been found to be mouldy. Such analogy does not encourage consideration of the binomial distribution.

This basic flaw in Hoyle and Wickramasinghe's reasoning was pointed out in a article in New Scientist in 1981[23] and it would not be necessary to repeat it here if the authors of Diseases from Space had shown any sign of developing their own thinking as a result of it[24,25.] Instead they have made repeated references to the arguments presented in that book as providing conclusive support for the cometary hypothesis.

As an illustration of the dangers of drawing rash inferences from contingency tables it is worth considering an epidemic at a boarding school which was similar to those presented in Diseases from Space and reported in the columns of New Scientist by Jennison, Butt and Byrom[26,27.] This concerns an outbreak of influenza in 1978 at the King's School Canterbury. In nine houses on a given site, and having an average of 51 pupils per house 61% of the pupils were infected (attack rates ranged from 37% to 84%). In a tenth house on another site with 59 pupils, none were infected. Jennison, Butt and Byrom had this to say about the epidemic, 'our own calculations cannot account for it by random chance.' What these calculations were is unclear since they were not presented. What exactly 'random chance' is or should be in this context and whether its definition can provide any relevant link to a model of person to person transmission is also uncertain. What can be conceded is that a very impressive chi-square value can be calculated for these data. Nicoll,

however, using chain binomials for which the probability of infection between individuals in the same house was allowed to be higher than the probability of infection between individuals in different houses, was able to find models for which nine was the commonest number of houses infected and with average attack rates exceeding those reported in the King's School epidemic and showing that apparently impressive contingency tables were easily generated[28.]

In fairness it has to be noted that this required extremely high ratios (e.g. 150 to 1) for within house to between house infection but her models assumed, in the absence of more detailed information on social geography, that every individual was capable of infecting each other. Because of the nature of the chain binomial model (which is not in fact a spatial process) equal values of infectivity would place an individual at greater overall risk of catching the disease from individuals in other houses than from those in the same house. The models Nicoll used, in fact are extremely parsimonious. It would not be unreasonable to consider infection between and within bedrooms and between and within classrooms and include interactions for these factors as well and since such a model must include the one she did consider as a special case the fit that would result could not possible be worse.

Parsimony in Modelling

Parsimony is not be found, however, in the Hoyle-Wickramsinghe model itself. In fact for none of the epidemics reported in Diseases from Space do they perform any probability calculations on the assumption that the cometary hypothesis is true, for the simple reason that the mode is insufficiently defined. Since they allow viral infall to be patchy at any scale required, since they allow that different buildings can offer different degrees of protection, since they allow that chance events like opening a window at the wrong time can affect the course of an epidemic, since viral particles from a given passage of a comet may be allowed to fall to earth over a decade if the data

require this[24], since comets may be of short or long period, since the debris from them may be localised or not, there is nothing that the theory cannot explain. One should hesitate a long time before adopting such a theory since the task of finding refutations will not be easy.

If clouds of viruses may be as heterogenous as you please the same is not true of human society, which is implicitly taken to be more regular than an ideal gas by the authors of Diseases from Space. It is interesting to contrast this attitude to human society with that of Neyman who, having developed some clustering processes from simple assumptions, delivers a warning about believing that these will be adequate for the analysis of an actual epidemic because of the varied locations, crowded or lonely in which infectious individuals may find themselves at key moments. He ends with the observation that, 'those statisticians who have a liking for applied problems of some delicacy may enjoy trying their hand at theory of epidemics.'[13]

Mixing and Analysis

It is worth considering carefully nevertheless whether there are any possible conditions as regards the organisation of human society and the nature of disease which could combine to make the analysis of Hoyle and Wickramasinghe valid.

For example, perfect mixing (as perhaps approximated to at a party), is a strong condition which would make the distribution of cases across space random. This would not, however, validate the contingency analysis because if individuals mix perfectly any classification of them by location is arbitrary, and whilst this arbitrariness guarantees random allocation under the null hypothesis it also has to do so under any alternative hypothesis and makes identification of process impossible.

A possible suitable combination would be a (presumed) highly infectious disease in a prison in which prisoners spent most of the time isolated in cells but came together for short periods of exercise. Under such conditions the

spatial classification by location of cell might be considered arbitrary under the hypothesis of person to person transmission but not under the cometary hypothesis if viral infall may be assumed to be patchy at an adequate scale and it can be hoped that there is a reasonable chance of the exercise areas and some of the cells being missed. Despite their common reputation it is doubtful as to whether such conditions are ideally replicated in Britain's boarding schools and whether it is reasonable (one is tempted to say fair) to shackle the conventional theory with so much regularity whilst allowing so much liberty to the cometary hypothesis.

The Development of the Debate

For the cometary debate, at least regarding statistics of epidemics, to develop further, a number of conditions would seem to be desirable. The first would be for Hoyle and Wickramasinghe to recognise the inappropriateness of their own analysis of the contingency tables presented in Diseases from Space and to adopt some of the stochastic models which epidemiologists had actually felt that theories of person to person transmission required them to use in the fifty or so years between McKendrick's pioneering work[29] and the appearance of Diseases from Space[5]. This will have the further effect of bringing them into contact with a considerable literature of disease modelling whose successes they will have to explain. (There is no space to begin to review these successes here but since the paper has already been cited, Bartlett's work on measles periodicity may perhaps be singled out[17]). Hoyle and Wickramasinghe may prosecute as they wish and will no doubt make their own judgements but mathematical epidemiology has to be permitted to make the defence. Secondly, because, the problem is one of deciding between different clustering mechanisms and because, therefore, it is unclear what sort of unusual pattern gives more support for the cometary hypothesis than for the conventional theory some explicit modelling is required for the cometary hypothesis itself. Thirdly it will be necessary to collect data which is richer in detail than that considered in Diseases from Space and which may have include classification by time of infection as well as by location and quite probably information on social relationships as well. Fourthly it will be

necessary for mathematical epidemiologists to consider the cometary hypothesis seriously and this they are unlikely to do until the proponents of the cometary hypothesis give mathematical epidemiology the same respect.

Finally, there is always the possibility, that developments in other sciences may make the statistical debate irrelevant, and decisive evidence for the cometary hypothesis may be discovered. In that case the statistical argument in Diseases from Space may take its place with Kepler's theory of the regular solids and Galileo's theory of the tides as a false milestone on the road to true enlightenment.

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