THE ROADS TRAVELED: OUR 50 YEAR JOURNEY

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We will be thinking, dreaming, and breathing statistics in this volume. To ensure we retain a balanced perspective on life, I refer you to the famous American Robert Frost's well known poem "The Road Not Taken" (see end of this article). With apologies to Robert Frost, rather than focusing on roads not taken, we shall briefly consider instead roads we have taken, or "The Roads Traveled", over the 50-year journey of our Journal and our Society.

In 1955 William Cochran gave an important Presidential Address under the title, "The 1954 Trial of the Poliomyelitis Vaccine in the United States". My reading of Cochran's address is that it was surely a compelling presentation, dealing as it did with a disease that was seemingly running rampant and which almost surely was capturing everyone's attention. As Cochran (1955) stated

> "this (vaccine) trial represents an important application of biometrical principles in the struggle against disease",

and expressed the view

> "that in terms of numbers of subjects the experiment may be the largest that has ever been conducted",

no doubt one of the major precursors of the many clinical trials studies today. Cochran described the plan of the study and gave some results, but also considered some of the major difficulties in the conduct of the trial, and it is here that analogies with current issues surrounding AIDS are particularly pronounced. What were some of these difficulties? Cochran lists:

(i) *Poliomyelitis is a relatively rare disease. The trials revealed there were 0.044% or 44 cases per 100,000 children in the 6-9 year old age range.* It is difficult to give figures for AIDS (though overall it is currently 0.14% of the U.S. population), but certainly AIDS is also a rare disease.

(ii) *The disease is difficult to diagnose. It was easy to make mistakes*, somewhat akin to the false positives or false negatives in detecting HIV infection. While the ability to diagnose HIV infection is improving, there is still a time delay between exposure and detection. Also, with respect to AIDS vaccines so far, some vaccines result in false positives on the HIV test and this has unfortunate social ramifications.

(iii) *The vaccination required three injections over a six-week period, with the consequence that some individuals dropped out before completion.* For AIDS, the expectation is that the vaccine's administration will cover multiple stages, though their actual timing and duration are not yet clear.

(iv) *The experiment subjects were children. Would parents give permission? Would the medical infrastructure, physicians, medical societies, etc., give and encourage cooperation*? The subjects for AIDS are not typically children. However, the question whether individuals will give permission for themselves to participate still pertains. Likewise, will society give such permission? Recall that even polio vaccines do not give 100% protection. While still unknown, the potency and ability of AIDS vaccines to protect appear to be very low for those vaccines developed thus far; so there is a real question as to how society will respond to any decision to pursue or not to pursue such vaccine trials.

(v) *Some biometricians had developed a pessimistic view of the prospects of success of any large trial with human subjects. Procedures necessary for statistical purposes may be viewed as functionally impractical, instructions could be misread or misinterpreted, records were incomplete and missing data abounded.* Today, however, in contrast, there are biometricians who would say this situation has reversed; that large simple trials are now very do-able and have been done, though not necessarily for vaccines.

To Cochran's five difficulties, we add a sixth which applies to AIDS, but not to polio:

(vi) Vaccines are targeted to specific virus types. Since for AIDS, viral strains differ across countries, a vaccine that may be successful in one country, may have a miniscule effect elsewhere. *This was not a problem with polio as the Salk vaccine was successful worldwide.*

Much as I myself would like to hear and read about the counterpart challenges arising in AIDS vaccine trials, or in the efforts to determine prevalence of HIV infection, or of any other specific topic that might capture our immediate interest and attention, that is not what I intend to do here. Rather, noting that 1994 marked the 50th year of the publication of *Biometrics*, what better time is there than now to journey down the roads along which biometry has traveled since Volume 1 in 1945?

My original goal was to read all 50 volumes , to trace the routes followed by researchers over the years. Needless to say, I become bogged down early, not because the road was difficult but more because I became totally engrossed in the papers themselves. Indeed, these early years' volumes are a most fascinating read. Were you to try the same exercise, you will not be able to escape the feeling that you are treading a historical path, one on which with each step (or paper) you become amazed repeatedly as to how much of today's standard familiar material has been associated with our statistical forefathers. While I certainly felt, and I believe you too will feel, compelled to pause to read these papers fully, the road is nevertheless fascinating as we are lured on and on with the intrigue of wondering what else lies around the corner, as we observe when, and by whom, basic material was first introduced.

As I set out on this journey, it soon became apparent there was neither time for me to read all of the 50 volumes nor time to share them with you. Therefore, after reading the first ten volumes, I decided to tackle the most recent ten years. This was quite a daunting task, and not just because of the large number of pages. Rather, it was the nature of the material itself as we are all too well aware. We could say the road had become an uphill trek; some might even say we were now scaling mountains complete with mountain-climbing ropes and equipment. However, on closer scrutiny I am not so sure that is an accurate portrayal of our journal as it stands today. For the reader with mathematical training, any one paper in their statistical specialty is reasonably easy enough to read, though it might take some effort to work through the mathematical details before comprehension dawns. What does seem more overwhelming, is the wide range of mathematical tools needed and the considerable time that is necessary in order to understand **all** of the papers; there are just too many subspecialities for one person to master all of them in their entirety. So rather than mountains to scale headon, there really are trails and back roads to traverse that will take us to our desired goals so long as we are patient enough to seek them out and then to travel up them.

Having said that in apparent and real defense of our mathematically oriented members, I do agree and sympathize with our members who are primarily trained in biology or agriculture or the like but who depend on statistical procedures as the primary tool in the design and hence the analysis and interpretation of experiments in their substantive field. Their contentious complaint is that in recent years *Biometrics* papers are far too mathematical to be read, and that furthermore they appear to be written solely from a theoretical standpoint, with the authors subsequently casting around for an example to which the theory can be applied after it has been developed.

Whether or not these claims can be substantiated or whether this is the prevailing format for the written presentation even when the theory was actually motivated originally by an application, is hard for me to distinguish. It is certainly true, however, that from my current perspective 50 years down the road, the early papers appeared to be driven entirely by the application. When the particulars of a specific problem ran up against the boundaries of available techniques, some researchers stopped, though often suggesting future directions along which new techniques could be developed, while others pressed on to develop the needed theory themselves. The universality of such newly introduced statistical methodology tended to come later.

However, whether or not this tension between mathematics and application focus is a matter of perception or merely of the written style, it is I believe healthy, since both are necessary components for the vitality and vibrant growth of our subject; but also it is not new. To illustrate, let us first retrace our steps to a paper by Davies and Hay (1950) on "The construction and uses of fractional factorial designs in industrial research" in which we read

> "Many papers have appeared during the past few years on this subject ... unfortunately for the industrial research worker [to which we can add the biological research worker], these papers written largely from a mathematical standpoint, have tended to mask the essential simplicity of these very useful and valuable designs".

This lengthy paper then went on to elucidate in a wonderfully expository presentation the construction and uses of such designs in research practice.

While that paper focused on a specific methodology, fractional factorial designs, its remarks were representative of many similar comments. The perception that our journal had become too mathematical was becoming quite pervasive apparently. Let me quote from C. I. Bliss in his 1958 account of the first decade of the Biometric Society and in particular his review of the role of the journal *Biometrics*:

> "One (of) the periodic complaints of our biological members (is) that the journal is becoming too 'high brow' statistically for them to understand, and the counter-complaint of the Editor that good biological, less technical manuscripts are hard to come by, despite numerous pleas for material. After all, editors cannot accept papers that are not submitted for publication."

This was in 1958, and echoes almost the same precise sentiments we hear today! Bliss did go on to admit that

> "over the years (*Biometrics*) has become more technical and advanced statistically",

though let me assure you that those papers were all quite easy to read compared with those of 1994.

Furthermore, and most interestingly in light of subsequent recent events, a 1953 proposal which emanated from the Belgium Region called for the start of

> "a second journal to be called *Acta Biometrica* with more emphasis on quantitative biology and less theoretical statistics, ..., and to draw primarily upon papers given at Regional meetings in continental Europe".... (The) proposal was discussed at length by members and Council, (but they) "were unable to solve essential details such as its editorial policy, relation to *Biometrics*, and financing, so that the proposal was never implemented."

The details of that discussion sounds remarkably familiar to those of us who participated in the recent debates following then-President Jonas Ellenberg's presentation to the Editorial Advisory Committee and to Council at the 1988 IBC in Namur, coincidentally in Belgium. He proposed a new journal specifically targeted as being applied (and not theoretical) in focus and with the facetious title *Statistics NOT in Medicine.*

Well, it may have been 40 years since the Belgium proposal in 1953, but in 1993 agreement was reached to move ahead with plans for a new journal called the *Journal of Agricultural, Biological, and Environmental Statistics (JABES)* to be published jointly by the International Biometric Society and the American Statistical Association with the first issue scheduled to appear in 1996. Its first editor is Dallas Johnson. Extracts from the Call for Papers strike a resoundingly familiar chord that has rung down through the decades: As the name suggests, the journal

> "... emphasises applications of statistics in agriculture, biological, and environmental sciences ... (seeks) articles of immediate and practical value to the applied workers in these fields ... to develop the interface between statistics and the biological sciences ... only applied papers will be considered [note the specific exclusion of theoretically focussed papers] ... expository, review and survey articles addressing broad-based statistical issues in the biological sciences will be valuable"...

Need I say more?! This should be a welcome addition and should address the needs and interests of many of our members.

The specific call of *JABES* for expository, review, and survey articles transports us back to the beginnings of our journey through *Biometrics*, as a quick glimpse of titles in Volume 1 reveals. As we set out, perhaps we should remind ourselves that our first two volumes were called the *Biometrics Bulletin*, which essentially combines the functions of today's journal *Biometrics* and the present-day *Biometric Bulletin*. Also, the *Biometrics Bulletin* was published by the Biometrics Section of the American Statistical Association out of which our Society was formed two years later in 1947. Bliss who chaired the Biometrics Section at the time bought the title from a Dr. Jellinek for $1. [Jellinek had begun a journal under that name in 1936 but it was discontinued after one volume of four issues (Fertig, 1984).] Bliss then changed the name to *Biometrics* beginning with the first issue in 1947. Also, whatever trepidations and uncertainties Bliss and Gertrude Cox, our first editor, might have felt in the early days, as adjudged by the cautionary comments in the Notes and News sections, these had totally dissipated by the time of Bliss's ten-year review. Indeed, while in the first year each issue tended to have just one major paper, by its third year several scientific articles appeared and *Biometrics* was clearly a fully-fledged and respected journal making important contributions to the scientific literature.

From its inception, our journal was designed primarily for biologists who saw statistics as a powerful tool in their work. Thus, we have in Volume 1, 1945 (*Biometrics Bulletin*)

No. 1: Some uses of statistical methods in medicine, J. R. Miner;

No. 2: Some uses of statistical methods in plant breeding, F. R. Immer;

No. 3: Statistical methods in forestry, F. X. Schumacher;

No. 4: Some uses of statistics in plant pathology, F. Wilcoxon;

No. 5: Confidence limits for biological assays, C. I. Bliss;

No. 6: Some applications of statistical methods to fishery problems, W. E. Ricker.

With the exception of Miner's paper which dealt with medical applications and tended to restrict attention to quite elementary statistical concepts such as the proportion of smokers who had coronary sclerosis compared with nonsmokers in the same age group (in this example, incidentally, drawing upon works of one of our well-known medically based forefathers Jo Berkson), with this exception, the early papers almost all proceeded down the path of agriculture broadly defined, using almost exclusively design of experiments techniques, including regression, in one form or another.

Wilcoxon's (1945a) paper is particularly interesting in that, when listing plant diseases, he makes specific reference to spatial spread, a problem which is still largely unsolved today but which is attracting attention from some of our current members, especially in the United

Kingdom and Australasia, for example, the nearest neighbor results of Besag and Kempton (1986), Gleeson and Cullis (1987), Cullis and Gleeson (1991), and Baird and Mead (1991). If we add Federer and Basford (1991), though not from the UK or Australasia, we will accord Federer the unique distinction of being singled out for signal contributions in both the first and fifth decade (but Basford is Australian). Here, I am restricting such examples to the *Biometrics* literature. To keep to such a restriction, however, is not totally wise, as to do so in this case would necessitate the omission of the fundamental paper of Wilkinson et al. (1983), these authors also incidentally hailing from the Australasian Region.

We noted that each issue started with a general expository article about statistics and its application or use in some field of biology. There was usually a second shorter article on a more specific topic; I draw your attention to but two of these, namely,

No. 4: A probit scale for slide rules, A. A. Bitancourt;

No. 6: Individual comparisons by ranking methods, F. Wilcoxon.

Wilcoxon's (1945b) paper is especially significant in that, although it is presented around the application of fly spray tests, we have the first paper in which a new theory (Wilcoxon rank sum tests) is introduced. The other paper from 1945 worthy of special attention because of its historical place is that of Bitancourt (a Brazilian, so we were truly international right from our beginning). He focuses on the slide rule as a tool.

In fact, there were many papers in these early years which dealt with easy or not so easy ways around computational problems and/or how the calculators of the day could be persuaded to obtain numerical results more efficiently. Further examples include

1948: Analysis of covariance and non-orthogonal comparisons, M. H. Quenouille;

1951: Asymptotic regression, W. L. Stevens;

1951: The calculation of χ^2 for an $r \times c$ contingency table, P.H.Leslie;

1952: The use of ranks in a test of significance for comparing two treatments, C. White;

1952: The computation of sums of squares and products on a desk calculator, J. M. Hammersley;

1952: Automatic machine method of calculating contingency χ^2, J. Skory;

1953: On the uniqueness of the line of organic correlation, W. H. Kruskal;

1953: Processing data for outliers, W. J. Dixon;

1954: Suggested desk calculator operations for computing moments by the row, F. M. Hemphill.

Stevens takes the regression equation $y = \alpha + \beta\rho^x$ which arises frequently, for example, in the study of animal (or species) growth y relative to age x, or crop yield y as a function of the quantity of fertilizer x; also, by suitable transformation, other regressions such as the Gompertz and the logistic follow this model. Today, it is no problem fitting this model to a set of data; but in 1951 this was still a formidable task. As Stevens says in his summary

> "The arithmetic labour of making a least-squares adjustment has proved so great that few research-workers appear to have attempted it ... it is therefore of immediate practical value to rationalise and reduce the arithmetic labour of finding efficient estimates of the three parameters. .... Tables are provided in terms of (a covariance) matrix for five, six and seven equally spaced values of x.

.... Worked examples are given to show how, with the help of these tables, the arithmetic labour need no longer be considered an obstacle".

White's paper deals with providing tables for a general case of the aforementioned Wilcoxon rank sum tests. Judging by his delightfully insightful comments surrounding the merits of this test, White, a physiologist, sorely felt the need of this procedure and his accompanying tables. However, perhaps the most intriguing comment is his small print acknowledgement (to the Royal Statistical Society) for a grant towards equipment. And we thought such requests for computers were a modern day invention! Lest we take ourselves too fast down the computational track, let me point out that Skory suggests that Leslie's hand-held method (that is, one exploiting tables of squares and reciprocals) be replaced by his machine method, where these fully automatic machines are the now obsolete desk calculators "Friden, Marchant, Monroe and perhaps others"! The older ones of us (including myself-I learnt on a Monroe) remember these well; the younger ones of us don't know what I am talking about!

One paper that does appear to anticipate the road ahead, however, is Kruskal (1953). He was concerned about the representation of a multivariate distribution by a single straight line, work which arose out of discussions about the application of statistics to paleontology. His so-called diagonal line of organic correlation was

"The unique line among those based on first and second moments which transforms properly under translation, change of scale, and omission of coordinates, and which in addition provides the proper directions of association; the unique line maximizing the probability of correct prediction"...

As we read through this paper, we are reminded of developments in the past 10-15 years in computational statistics surrounding topics along the lines of projection pursuit, grand tours, etc.

In the paleontology example, typical variables include skull length, cube root body weight, logarithm of antler length, etc. When the quantitative characteristics take the form of logarithms, the biological term "organic correlation" line is called an "allometric" line, a term which appears frequently in the biological literature. Furthermore, Kruskal points out that when there are substantial errors in measurement, the problem becomes extremely difficult. Indeed, this is still a difficult problem as we saw in a paper by Schmid et al. (1993) who fit an errors in variable allometric model to a censored data set dealing with goldenrod plant reproduction using the Gibbs sampler, a very recently developed computational method.

So, we started out on this particular phase of our journey bouncing over and through the ruts of the hand-held calculator, a slow ride but nevertheless making progress, past the development of statistical computer packages which we have not visited here, though Dixon's (1953) paper gives hints of how these were to unfold, through to the present when such computational aids are commonplace. But, the present also brings us the emergence of new methodology which could not have been conceptualized, let alone have arisen, without the computational power and resources of the computer itself. Examples that spring to mind include the projection pursuit and its derivatives, the bootstrap, imaging, Gibbs sampling, and multimedia. Before leaving this topic, as an aside, apropos of our earlier discussion of mathematical versus nonmathematical contributions, Kruskal's paper was quite theoretical, replete with Assumptions and Criteria, Theorems and Proofs, without a worked example in sight. Yet, his paper really is a forerunner of important computer methodology several decades later.

The pattern of featuring a review type article continued into the second year, although with a slightly different perspective. Thus, we have in Volume 2, 1946

No. 1: The estimation of variance components in analysis of variance, S. L. Crump;

No. 2: Statistical methods in cereal chemistry, C. H. Goulden and A. E. Paull;

No. 3: Missing-plot techniques, R. L. Anderson;

No. 4: Statistical methods for an incomplete experiment on a perennial crop, G. W. Snedecor and E. S. Haber;

No. 5: Measurement of virus activity in plants, W. C. Price;

No. 6: An approximate distribution of estimates of variance components, F. E. Satterthwaite.

These papers do contain more formulae though they still are basically review type articles. Crump separates out fixed effects and random effects models and provides the rules for obtaining the relevant expected mean square terms. Satterthwaite picks up from Crump and introduces his psuedo-F test whereby a variance is estimated by a linear combination of mean squares. Anderson presents a nice summary of formulae required to estimate missing observations. From my perspective today, it seems that these papers had to have had a great impact when originally published, especially among the applications oriented researcher.

Indeed, these first issues contain a wealth of marvelous examples of all descriptions, still useful today for those of us teaching design classes to biological and agricultural sciences students; not only are the data provided in seeming completeness but also there is usually an extended discussion of aims and goals, the relevance and importance of the experiment, as well as the subsequent interpretation and usefulness to the scientist. Since the early work in design was accomplished in the 1920s and 1930s, we do not see too much of the very basic designs though they do appear frequently in the broad review type articles dealing with "Statistics in ... forestry/fisheries/animal breeding/...". However, our journey through the first decade does bring to us many new designs as well as elaborations or refinements of the basic designs for situations in which the original simplifying assumptions do not hold.

Thus, we enjoy articles on lattice designs and their many variations such as cubic lattice squares, a series of papers on prime power lattice designs by Kempthorne and Federer (e.g., 1948) and Federer (1950), and rectangular lattices by Harshbarger (1949) and Harshbarger and Davis (1952); covariance (Finney, 1946); several papers on aspects of balanced incomplete block designs including confounded BIBD's by Bliss (1947) and partially balanced incomplete block designs by Nair (1952, which is a long theoretical treatise building upon his fundamental paper with Bose; Bose and Nair, 1939), and doubly balanced incomplete block designs (Calvin, 1954). There is a new model by Sophia Marcuse (1949) on optimum allocation in nested designs; measurement errors (Bartlett, 1949); chain block designs (Youden and Connor, 1953) and thence generalized chain block designs (Mandel, 1954); factorial designs for proportional data (Dyke and Patterson, 1952; Fisher, 1954), analysis of covariance with unequal cell numbers (Hazel, 1946); balanced partial confounded designs, cross-over designs,and so on. To these we add a considerable body of papers dealing with taste testing, starting with the seminal paper of Hopkins (1950) and reviewed by Bradley (1953). Sequential analysis enters our literature with a test for the negative binomial distribution for a fisheries application (Oakland, 1950). Finally, we mention Tukey's (1949) paper on comparing means in the analysis of variance, the impact of which we are all keenly aware.

Other papers focus on the "hows" and "whys" of using appropriately specific statistical methods. For example, the Goulden and Paull (1946) paper featured above includes a very nice discussion of the advantages of using factorial designs, and their views that covariance as a technique was "proving extremely useful" and that the method of fitting polynomials (which for them meant linear, quadratic effects components of the treatment sum of squares, and likewise for the interaction terms) was "proving of considerable value"; such views were indeed timely for the day. Also timely - for then, and still for today - was their stress on the importance of an interactive collaboration between both the (agricultural) researcher and the statistician. Goulden and Paull's paper reflects much of the learning and instructional nature typical of many of the early papers. Later, Jacob (1953) noting the rapid development of what seemed to be extremely complicated designs, elucidates in exemplary fashion the use of one such "complex" design, the split-plot half-plaid square design, using extensive data from a field irrigation experiment on fertilizers and potato varieties.

Perhaps, however, unarguably the finest set of papers is the following, from 1947:

- (i) The assumptions underlying the analysis of variance, Eisenhart, 1-21;
- (ii) Some consequences when the assumptions for the analysis of variance are not satisfied, W. G. Cochran, 22-38;
- (iii) The use of transformations, M. S. Bartlett, 39-52.

Eisenhart introduces his treatise with the remark that

> "analysis of variance ... today constitutes one of the principal research tools of the biological scientist, and its use is spreading rapidly in the social sciences,

the physical sciences, and in engineering",

a remark as applicable today (1994) as it was then in 1947. He singles out many aspects but one in particular which caught my attention concerned

> "the failure of most of the literature on analysis of variance to focus attention on the distinction between problems of the fixed effect model and problems of (random effect models) ...."

Given the failure of many of the contemporary statistical packages to accommodate these differences, a repeat of this paper might well be advisable. Indeed, all applied researchers, and those of us who teach such students, would be well rewarded by re-reading these original sources. Each is an illuminatingly clear exposition replete with numerous examples to illustrate the principles involved. Modern textbooks certainly include what amounts to summaries of many of the basic concepts featured in these three papers, but equally there is much that has been lost over the years.

To this set of three papers, we should add a fourth one, from 1954, namely,

Some methods for strengthening the common χ^2 tests, W. G. Cochran, 417-451.

Here, Cochran (1954a) demonstrates at length and again with numerous examples, how the "general rule" to group neighboring classes when the expected frequencies are less than five, is too conservative, and he goes on to provide a set of guidelines about what minimum expectations are recommended for use in a variety of settings; for example, for unimodal distributions such as the normal or Poisson distributions, grouping is carried out so as to achieve a minimum expectation in each tail of at least one (i.e., not the rule of "five").

Finally, it would seem that Cochran's (1954b) work on, The combination of estimates from different experiments, W. G. Cochran, 101-129, though directed at a series of design experiments, anticipates the meta-analysis concept of today.

If most of the titles and discussion so far have focused on design and agriculture, it is because these dominated the scenery in our first ten years. Indeed, three of the four Special Issues during this period focused on design (namely, analysis of variance in 1947, components of variance in 1951, and analysis of covariance in 1957). The fourth was a Fishery Reprint Series from 1949.There was a little, albeit comparatively very little , work in medical applications. Even the research on bioassays of the Bliss and Finney variety tended to come from agriculture, though that of Berkson did evolve from a medical setting. Despite the fact that the entire fourth issue of 1949 was devoted to biological assays, work on survival analysis, dose response curves, clinical trials and the like, were infrequent travelers in the early days though they did join the entourage at an increased pace in the second decade. However, in contrast, the last 20 years have seen a real role reversal with these topics and their medical applications, as dominating today as were design and agriculture yesterday, with design papers making considerably fewer appearances in recent volumes.

This observation does perhaps give us cause to pause and reflect upon just where the future of survival analysis, clinical trials, and the like will take us. These past two decades have indeed been witness to a plethora of activity, work motivated in part, but certainly not entirely by the war on cancer and the need for pharmarceutical companies to win government and market approval for their products. As someone not intimately involved with these issues on a daily basis, I have to wonder if the major theoretical statistical problems haven't been resolved, and that it is their implementation and use both here in the medical world and into entirely new areas of application, that will now take center stage. To keep with our traveling metaphor, are we at the point where the highway has been built, along which travel is relatively easy, but where we still need a license to drive, the license in this case being expertise and training in clinical trials, say? We have certainly seen this phenomenon before with, for example, experimental design, decision theory, even sequential analysis, though in this latter case it is more a consequence of the mathematical deadends, areas which enjoyed sustained activity with highly productive and very useful results, but where the former vitality has been replaced by a renewed vigor in new directions.

As we speculate on our possible future highways, may we content ourselves with a brief look at two topics both of which were fellow travelers in our first decade. As we consider aspects of these, in addition to the initial and recent past volumes of *Biometrics*, we also draw upon Levin (1992) who outlines some of the challenges and opportunities of the interface between mathematics and biology. Recognizing that statistics grew largely out of the biological sciences, Levin, interprets mathematics in his context to be primarily statistics but also differential equations.

One area falls under the general rubric of genetics. An article on genetic changes in the fruit fly species *Drosophila Pseudoobscura* (Dobzhansky, 1945) appeared in the very first issue; this fruit fly species appeared often and we still see papers on *Drosophila* today. There were several articles by Fisher, as might be expected, including his Founding Presidential Address on a theory of genetic recombination (Fisher, 1948) at the Inaugural International Biometric Conference. Primarily, articles were prompted from agriculture, poultry and animal science, such as crop, plant and animal breeding, species selection, and also genetic linkage problems. Human genetics was present though not to any great extent.

However, it is this latter area under the Human Genome Project and related research which is now attracting enormous attention. Furthermore, with modern computer sophistication, population and molecular geneticists have totally changed the way they approach their art. As Levin (1992) suggests

> "Attention to the human genome project and its great potential often obscures the fact that theoretical work is essential to efforts aimed at sequencing and mapping all genomes, human and nonhuman, animal and plant. Without the mathematical and statistical underpinnings and computational advances, such efforts will be severely limited; with these methods, we are poised to make dramatic advances".

Porter (1986), in his history of statistics, suggests that

> "quantitative genetics remains the best example of an area of science whose very theory is built out of the concepts of statistics".

New techniques have to be developed, especially in exploratory data analysis, computer graphics, stochastic nonlinear dynamical systems, etc. Some of these same statistical developments will be sought for organismal, as distinct from cellular and molecular, biology. Here, we enter the world of neuroscience and the now familar neural networks. Yet, this too has links with our first decade. Neural nets were described by McCulloch and Pitts (1948), and came up in Reid's (1953) review of stochastic processes in biology and its application to the central nervous system. Limited by a lack of adequate computing power, the early authors were unable to achieve very much beyond defining the problem. Today, they are not so hindered, though they would want to become conversant with techniques such as stochastic differential equations and image reconstruction methods, among others. Some of the most frequently occurring (known) theoretical tools buried behind these applications are those found in stochastic processes and in particular Markov processes and Markov chains, though even there statistical inference methodology for such processes is still virtually nonexistent for the needs at hand.

In a slightly different direction, stochastic processes also constituted the central core of a second body of work, that in epidemic and population modelling, including some work presaging contemporary ecology, which work enjoyed quite a deal of visibility in the first decade of our journal but which subsequently saw a declined level of activity, only to be reactivated to unprecedented levels again in the recent decade.

Early population models were deterministic in their formulation. It was Feller (1939) who drew attention to the fundamental fact that the processes being modeled were essentially probabilistic, which led to the reformulation of population modeling in a stochastic framework, typicaly as some variation of birth and death processes. While the deterministic models were formidable enough to solve, requiring sophistication in differential equation techniques, their stochastic analogs become even more forbidding. Linear birth and death models are relatively easy to solve, but stochastic models for most epidemic and population processes are nonlinear. The resulting differential, or partial differential equations, were not amenable to the usual solution techniques. However, our early years did see significant papers by, e.g., Chassen (1949) who tried to estimate an infection interval, Reid's (1953) review paper of stochastic models in biology, the chain biniomial results of Almond (1954), and the Lynx predator-prey analysis of Moran (1950). However, the intractable mathematics, and the lack of sufficient computer resources, would largely explain why these topics have lain in hibernation until recently.

With the advent of the AIDS epidemic, the resurgence of interest is evident and there are numerous contributions in *Biometrics* alone, e.g., Brookmeyer and Gail (1987), Brookmeyer and Liao (1990), and Solomon and Wilson (1990). Also, computer power has expanded, though the algorithms contained in most mathematical packages are still very limited in what they can achieve. New techniques in nonlinear ordinary and partial differential equations as well as differential-difference equations must still be developed. Even more important is the demand for statistical methodologies such as model fitting, parameter estimation, etc. The renewed interest goes well beyond AIDS, however, and includes, for example, influenza, measles, and malaria, such as, e.g., the work of Addy et al. (1991) and Haber et al. (1988), who consider influenza, and Nedelman (1988), who studies the Garki malaria data. These are human diseases.

There is also a considerable amount of work being done currently in plant, animal, and species epidemics, though much of this appears in the agriculture literature rather than in our immediate literature or *Biometrics* per se. This paucity of papers in our literature is a pity, as there is a lot of interesting and excellent work here. Indeed, a June 1995 issue of *Science* featured "the emerging world of Plant Science". Again there are links with our first decade. There is a nice treatment of a disease in plants in our early literature when Bliss and Fisher (1953) fit the negative binomial and Neyman contagion distributions to the spread of red mites in apples; and Beall and Rescia (1953) use the Neyman contagion distributions for a number of data sets, including the corn-borer, potato beetle, black scale (insects), bollworm in maize, etc. Perhaps more importantly for us as biometricians today, we have the opportunity to apply and to develop statistically sound methodologies for these diseases, especially since to date the focus has been on the mathematically easier deterministic model formulations. To these we add the problems of spatial spread; and to both temporal and spatial problems, there are problems of scale to be tackled.

Related but different methodologies arise when dealing with issues surrounding the environment whose emergence as an issue became apparent in the early 1970s, including, for example, ecology, global change, biological diversity, oceanography and meteorological data. Spatial techniques, though present for a few years now, primarily arising out of the geosciences, have more recently been spurred on by the demands of the environmental train, which demands will open up new opportunities for biometricians. Recent developments in remote sensing and in geographical information systems are important foundations but are only a start, and constitute only one direction in these endeavors. Changes in the social and economic conditions, especially in transition countries and developing countries, also provide a wealth of statistical problems demanding our attention and expertise, much of which will require new methodologies. The launching of Deep Flight I (a kind of underwater aircraft scheduled for late 1995) and its successors to scour and explore the ocean floor will doubtless prompt new growth in what can be termed "sea-floor biology" necessitating innovative developments in statistical methodologies to deal with the resulting new-found knowledge.

The immediate applications, of which there are several, may give the appearance that we will be traveling down a large network made up of many different roads, and in one sense we are. However, in another sense, these numerous applications are but many scenarios of the same broad highway, different scenery perhaps at differing locations and certainly different types of vehicles. Whatever mantle the specifics may don, our highway and our superhighway to the future - and by superhighway we do include its contemporary reference to computer technology and communication - promise us an exciting ride.

To digress for a moment, as we are propelled down the information superhighway seemingly out of our own control at times, it behooves us to ponder not only where that road is taking us but also how we may participate in the accompanying debates in order to be better prepared to utilize, but also to fashion and to contribute to the new technologies in meaningful ways. Earlier, we alluded to scientific advances that developments in computer capabilities have and will bring to statistics. However, it is conceivable that nonscientific advances, under the broad rubric of communication, will bring even more radical changes and have an even greater impact on our lives and our professional activities. For example, those of us connected to electronic mail and electronic transfer of information marvel at the ease of contact with members elsewhere; we wonder how we managed when limited to phone and paper transfer of information. The World Wide Web expands this facility further and leads to questions surrounding the need to appoint "electronic" editors (as distinct from the "scientific" editors of journals).

In his review of our Society's first decade, Bliss (1958) entertained some possible solutions to the difficult problem of tracking down biometrical literature which by its very nature appeared in a wide variety of substantive fields journals and outlets and not only in our own journals; this today is still a formidable task. Fortunately, as those of us who have luxuriated in the delights of having entities such as *Current Index to Statistics* online can attest, as more and more material is transferred to the electronic media, such difficulties will become a fading memory, albeit 50 years after Bliss's efforts.

Likewise, in a different direction, electronic publishing is now firmly stationed along our highway, at least as an issue with which many are grappling. By this I do not mean the electronic submission of manuscripts and/or the review process, though these steps too have their attendant issues, which issues are now largely solvable even if implemented to varying degrees across different journals and disciplines. Rather, I refer to the publishing of the journal itself on the electronic media, as distinct from the current hard copy which arrives on our desk. There are technological, legal, and ethical difficulties still to be resolved on this front. The questions are many but for most of us the answers are quite elusive. Just as a few centuries ago, the world witnessed the printing press bring radical changes to the parchment "press" of its day, so too are we in the throes of a similar radical transformation of the communication and dissemination of knowledge and information today as we evolve into an "electronic press". Some of us step aboard this train with great trepidation and some of us do so with intense excitement; none of us has the option of staying behind(!), though we will join it at varying stages of its journey. There would be few of us able or bold enough to predict where this will station us in the next millennium, our statistical prediction methodologies developed over the past 50 years notwithstanding. Most of us, however, would confidently predict that the modus operandi of our professional lives, both scientifically and nonscientifically, will be irrevocably transformed.

In closing, let us return to our present journey. *Statistics, biostatistics, biometry* . . . our discipline grew out of the biological sciences. Our Society has played a pioneering role though certainly there were other riders on the train with us. Statistics is an indispensable tool in the pursuit of the scientific chase. We still of course have to promote good statistical thinking with our fellow researchers in other disciplines, a continual effort until statistics is seen as an integral thread in the fabric of their disciplines. Theoretical and applied statisticians including biological scientists must travel in partnership, exchanging information and experiences for constructive progress to be assured.

These principles are as applicable today as when our founders established our Journal and our Society as evidenced by the vision expressed in our Constitution which begins with

> "The International Biometric Society is an international society for the advancement of biological science through the development of quantitative theories, and the application, development and dissemination of effective mathematical and statistical techniques"... .

From our very inception, through our growing years, to the present middle-age status of our 50-year-old journal, the interdisciplinary collaboration between statistician and biologist has indeed been an exciting, fruitful, and productive journey. However successful this journey has been, the past now lies behind us. We stand here poised in the present as we step forth into the future. The opportunities are vast, and the challenges are unlimited, but, they are rewarding.

Acknowledgement

This is essentially the 1994 Presidential Address delivered at the 17th International Biometric Conference in Hamilton, Ontario, Canada; see Billard (1995). The current version includes a few additional highlights from our 50 year journey as well as some thoughts and speculations about possible future travels in biometry.

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